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CONTENTS

OSTEOPERIOSTEAL BONE GRAFTS 161
GEORGE MORRIS DORRANCE, M.D. ..... PHILADELPHIA, PA.

BIOPSY BY NEEDLE PUNCTURE AND ASPIRATION 169
HAYES E. MARTIN, M.D., AND EDWARD B. ELLIS, M.D. ..... NEW YORK, N. Y.

TRAUMATIC LESIONS OF THE BRACHIAL PLEXUS 182
THOMAS A. SHALLOW, M.D. ..... PHILADELPHIA, PA.

THE CAUSE AND ELIMINATION OF REACTIONS AFTER INTRAVENOUS INFUSIONS 195
LEE RADEMAKER, M.D. ..... PHILADELPHIA, PA.

HYPERPARATHYROIDISM 202
JOHN DE J. PEMBERTON, M.D., AND KENNETH B. GEDDIE, M.D. ..... ROCHESTER, MINNESOTA

THE TREATMENT OF ACUTE EMPYEMA THORACIS 212
LEWIS CHANDLER FOSTER, M.D. ..... NEW HAVEN, CONN.

A BACTERIOLOGICAL AND CLINICAL STUDY OF GASTRIC ULCER 222
EDWARD WATTS SAUNDERS, M.D. ..... NEW YORK, N. Y.

ACUTE ULCERATIONS OF THE STOMACH IN CHILDREN 234
BENJAMIN RICE SHORE, M.D. ..... NEW YORK, N. Y.

ANNULAR PANCREAS INVOLVED IN ACUTE HÆMORRHAGIC PANCREATITIS 241
OSBORNE ALLEN BRINES, M.D. ..... DETROIT, MICHIGAN

SUBACUTE PANCREATITIS OR SO-CALLED ACUTE ŒDEMA OF THE PANCREAS 248
DEWITT STETTEN, M.D. ..... NEW YORK, N. Y.

ECTOPIC SPLEEN CAUSING INTESTINAL OBSTRUCTION 263
ARTHUR A. SALVIN, M.D. ..... NEW YORK, N. Y.

INTESTINAL OBSTRUCTION 270
LOUIS ANTUPIT, M.D., AND DANIEL F. SULLIVAN, M.D. ..... HARTFORD, CONN.

THE USE OF PERFRINGENS ANTITOXIN IN INTESTINAL OBSTRUCTION 277
JOHN PAUL NORTH, M.D. ..... PHILADELPHIA, PA.

THE PREVENTION OF PERITONEAL ADHESIONS BY AMNIOTIC FLUID 281
JAMES T. LACEY, M.D. ..... PHILADELPHIA, PA.

PATHOLOGICAL STUDY OF POSTERIOR VESICAL NECK OBSTRUCTION 294
ALBERT E. BOTHE, M.D. ..... PHILADELPHIA, PA.

TRANSACTIONS OF THE PHILADELPHIA ACADEMY OF SURGERY 300
STATED MEETING HELD MARCH 3, 1930.
STATED MEETING HELD APRIL 7, 1930.

BRIEF COMMUNICATION: *Joseph*: Insulin in the Treatment of Non-Diabetic Bed Sores 318

BOOK REVIEW: *Beer and Hyman*: Diseases of the Urinary Tract in Children 320

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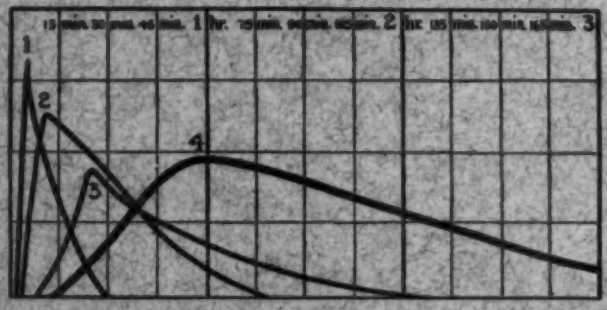

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ANNALS *of* SURGERY

Vol. XCII AUGUST, 1930 No. 2

OSTEOPERIOSTEAL BONE GRAFTS *

By George Morris Dorrance, M.D.

of Philadelphia, Pa.

FROM THE LABORATORY OF RESEARCH SURGERY, UNIVERSITY OF PENNSYLVANIA

In 1926, Dr. George Wagoner and I proved by a series of experiments that it was possible to produce fixation of a joint in dogs by an extra-articular osteoperiosteal bone graft.[1]

A patient with a recent fracture of the internal condyle of the femur was referred to me. (Fig. 1.) The patient was admitted to Saint Agnes Hospital on September 6, 1927, and operated upon on December 28, 1927. This patient had an old infected arthritis of the knee-joint and on account of the pain and disability, I decided to ankylose the joint. It would have been difficult in this particular case to have performed a whole thickness graft and an extra-articular osteoperiosteal bone graft seemed to be indicated. (Fig. 2.)

The extra-articular graft was performed by making an incision in the lower portion of the thigh above the capsule of the knee-joint and extending this through the skin, fascia and muscles to the femur. A second incision was made over the upper end of the tibia and extended through the skin and fascias to the bone. By undermining the skin between these two incisions a subcutaneous tunnel was made. The periosteum over the exposed surface of the femur and the tibia was elevated and the surface of the bone chiseled or rongeured off, exposing roughened bone. An osteoperiosteal graft was obtained from the tibia and wrapped in rubber dam. One end of the graft was introduced into the wound over the tibia, then through the tunnel to the wound on the lower end of the thigh. The rubber dam was removed and one end of the graft was secured to the femur and the other end to the tibia. The wounds were sutured and the leg was placed in a plaster case. (Figs. 3, 4, 5, 6, 7.)

The growth, as shown in the X-ray picture, illustrates what occurred better than any description could. The joint is now fixed and the patient walks without a cane or crutch.

The thickness and strength of a bone graft depends upon the amount of weight and strength that is placed upon it. I am sure there is a distinct indication in joint disease for an extra-articular osteoperiosteal bone graft. It is a simple matter to remove this bone graft at any time in the future if it becomes necessary. Some years ago, I had the opportunity of observing a rather large number of bone grafts performed for loss of structure of part

*Read before the Philadelphia Academy of Surgery, March, 1930.

[1] Transactions of American Medical Association, Section in Surgery, 1926.

FIG. 1.—X-ray of joint before bone graft.

FIG. 3.—Time of operation.

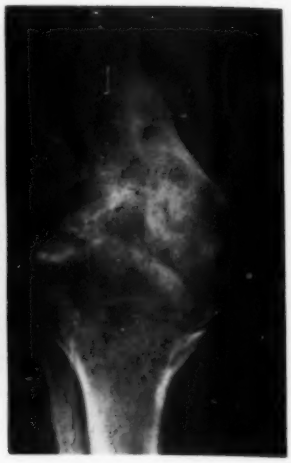

FIG. 4.—Three months after operation.

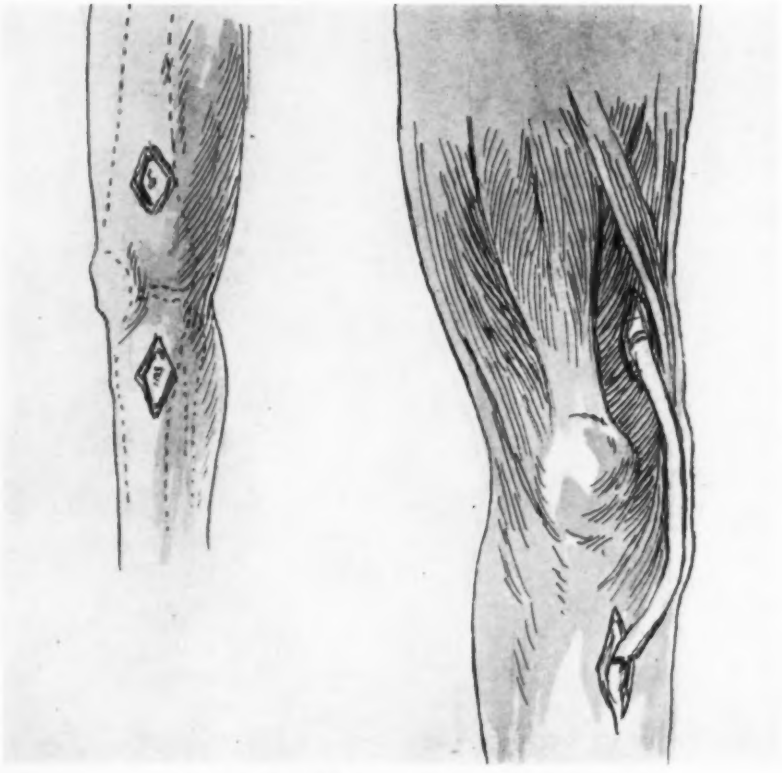

FIG. 2.—Extraarticular osteoperiosteal bone graft.

FIG. 5.—Six months after operation.

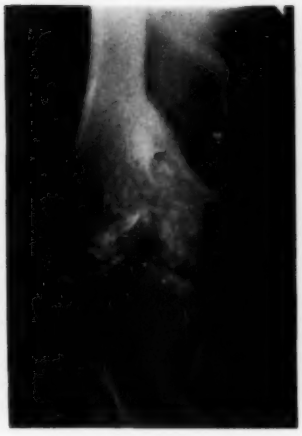

FIG. 6.—Nine months after operation.

FIG. 7.—One and one-half years after operation.

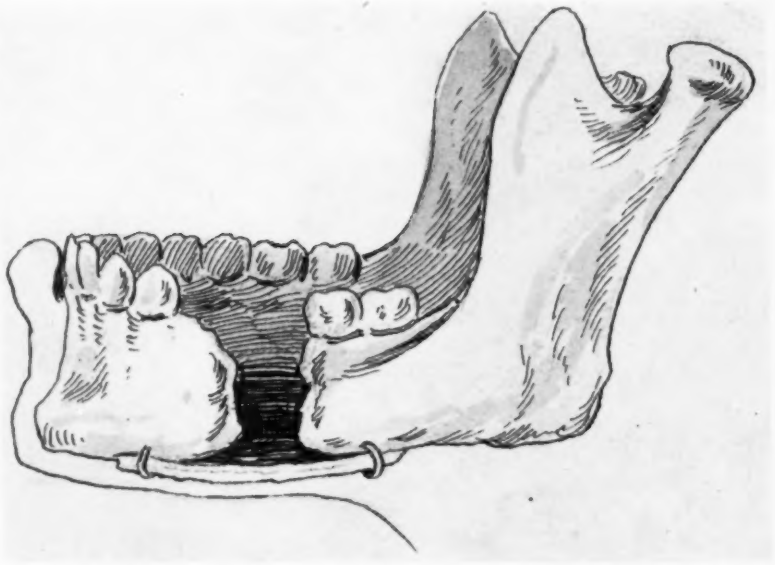

FIG. 8.—Subcutaneous osteoperiosteal bone graft.

of the lower jaw and for ununited fractures of this bone. Some of the surgeons used full thickness bone grafts from the tibia, rib, or crest of the ileum. Others used a pedicle flap with bone attached and still others used an osteoperiosteal graft. Some failures were noted in all types. The pedicle flap containing bone was the most satisfactory where it was possible to use it.

What were the reasons for these failures? First, the ends of the ununited parts of the bones were only too frequently thin and sclerosed. Second, in exposing the ends of the bone, one frequently penetrated into the oral cavity. Third, infection was the most frequent cause for failure. In osteoperiosteal grafts, perhaps this was due to the fact that the graft was laid in the wound without fixation.

Osteoperiosteal grafts always appealed to me on account of the ease and simplicity of application. In the jaw they are especially indicated as they readily conform to the curve of the bone. (Fig. 8.)

The subcutaneous method of performing a bone graft is the easiest and causes the least damage if a failure ensues. The portions of the bones where the grafts are attached are normal while the ends of the bones are hard and sclerosed.

In 1928, I thought if we bridged the gap from one side of the jaw of a dog to the other, it would be a good experimental test of the value of the subcutaneous osteoperiosteal bone graft. Accordingly the skin was incised over one side of the jaw and also on the opposite side. The bone was exposed, the periosteum elevated and the bone roughened. The skin covering the area between the two halves of the jaw was undermined and a subcutaneous tunnel was made to connect the two incisions. An osteoperiosteal bone graft was raised from the tibia and wrapped in rubber dam and then passed through the tunnel. The rubber dam was then removed and each end of the graft placed over the roughened bone and held in place by suturing the soft tissues. Note that the bones were not drilled.

In 1928, we performed three of these experiments but none showed complete union on both sides.

Dog No. 45.—Operated upon June 26, 1928. Killed 226 days later. Photograph shows the result of graft attached at one end only. (Fig. 9.)

Dog No. 38.—Operated upon June 27, 1928. Killed 225 days later. Result similar to dog No. 45. (Fig. 10.)

Dog No. 17.—Operated upon June 28, 1928. Killed 190 days later. At autopsy it was found that the entire graft had been absorbed.

Why did the grafts in dogs Nos. 45 and 38 fail to unite at one end?

First, we attempted to do what is recommended, that is, to lay the graft in place against the bone and hold it by suturing the soft tissues over it. We now think the graft should have been secured to the bone by wire or gut ligatures. The external surface of the bone should have been thoroughly removed, after elevating the periosteum. Second, the muscles between the halves of the jaw kept the grafts in almost constant motion.

FIG. 9.—Photograph of specimen of dog No. 45.

FIG. 10.—Photograph of specimen of dog No. 38.

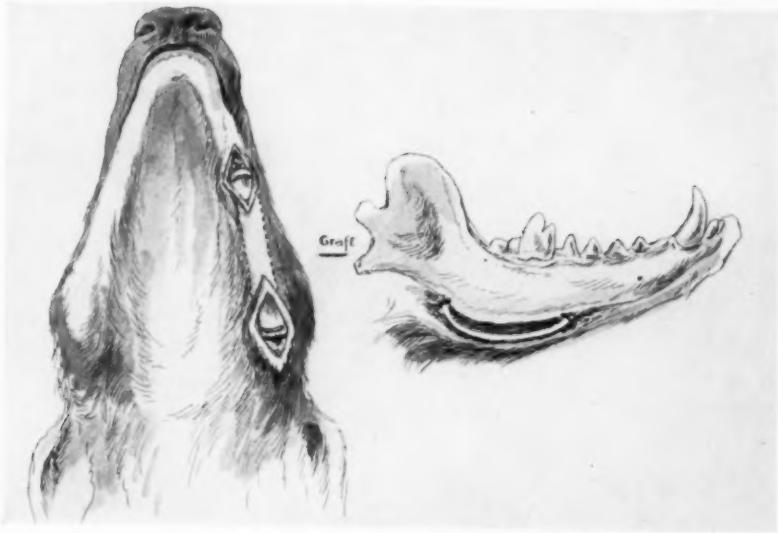

FIG. 11.—Method of performing subcutaneous bone graft.

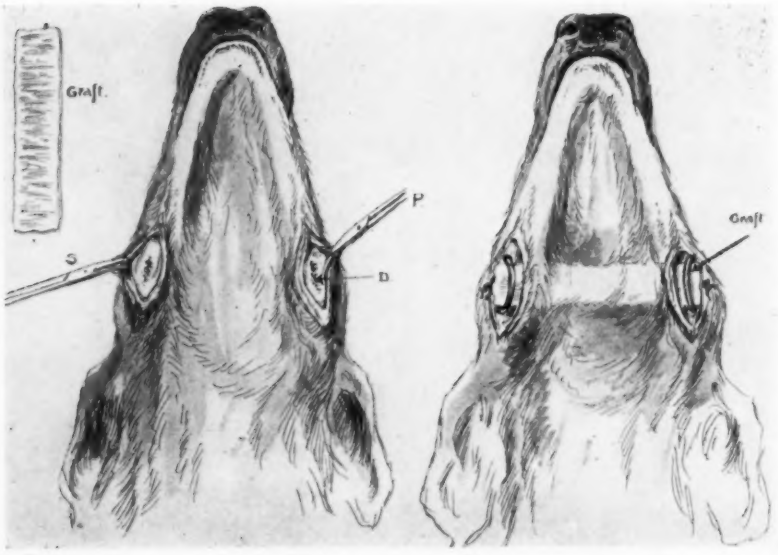

FIG. 12.—Method of performing subcutaneous osteoperiosteal bone graft.

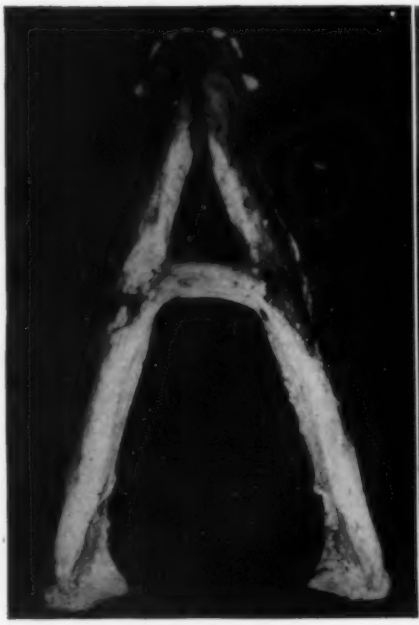

FIG. 13.—Photograph of specimen of dog No. 56 from below upwards.

FIG. 14.—Photograph of specimen of dog No. 56 from above downwards.

In two other dogs, we made two incisions over the same side of the jaw—one incision at the angle and one in the canine tooth area. (Fig. 11.)

A subcutaneous tunnel was made connecting these two incisions. The periosteum was elevated and the bone roughened in each area. An osteoperiosteal graft was obtained from the tibia and wrapped in rubber dam. This was introduced into the tunnel and after removing the rubber dam, the ends of the graft were forced under the periosteum and the soft tissues sutured over them.

This was done in dogs Nos. 255 and 439. This is as nearly an ideal arrangement for a bone graft as is possible.

Dog No. 255.—One hundred days after the bone graft operation an autopsy showed that both ends of the graft had united to the jaw bone. The graft was excellent.

Dog No. 439.—The graft was in place for thirty days when, on account of distemper, the dog had to be gassed. The graft was growing but the anterior end seemed to be free.

FIG. 15.—Photograph of specimen of dog No. 49.

FIG. 16.—X-ray plate from dog No. 58.

In two dogs an osteoperiosteal bone graft was placed in the fascia or muscle but not in contact with bone. In both cases the grafts were absorbed. This confirms a fact long established by Ollier that a bone graft not in contact with bone is absorbed.

As the bone graft experiments performed in 1928 were not satisfactory, we decided to repeat the experiments in 1929, but instead of laying the grafts in place we carefully sutured them to the denuded bones with silver wire. (Fig. 12.)

Experiment No. 1: Dog No. 56.—An incision was made on each side of the jaw and a subcutaneous tunnel connecting the two incisions was made. The periosteum was elevated, the outer table of the bone removed and the bone drilled on each side. An osteoperiosteal graft was introduced and held in place by silver wires.

Note the perfect graft which is good and thick and strong.

The time which elapsed between the operation and the autopsy was 211 days. (Figs. 13, 14.)

Dog No. 49.—Graft was in place for 213 days and remained attached to the left side only. Why did it remain attached to one side only?

From examinations during life and at time of autopsy, it is my opinion that the continuous action of the muscles caused the non-union of one end. (Fig. 15.)

Dog No. 58.—Graft was in place for 233 days. Before autopsy, the graft seemed to be attached on both sides. At autopsy, a little movement was present on the right side of the jaw. When the specimen was returned after maceration it was found that the graft had been attached at each end by fibrous tissue. (Fig. 16.)

Dog No. 43.—The same technic was followed. The graft was in place for 247 days. X-ray plates showed good growth and firm union on both sides. At autopsy, the specimen revealed a good, strong, well-united graft. (Fig. 17.)

FIG. 17.—Photograph of specimen from dog No. 43.

The results of the four bone grafts in 1929 were as follows: Two gave perfect results; one showed a good growth of bone but this was not firm at the ends; one showed a graft to be present but united at one end only; after seven months, we have three perfectly successful grafts and one with only one end complete.

Why are they not all perfect? I do not know. I can only attribute the non-union of the frequent movements due to pull of the muscles.

CONCLUSIONS

Full-thickness bone grafts are used and generally considered to be best, but osteoperiosteal bone grafts are indicated in selected cases.

My observations from both experimental and clinical studies are that the ideal conditions for successful osteoperiosteal bone grafts are:

1. The osteoperiosteal bone graft should contain a good supply of bone with the periosteum. The periosteum that is stripped from the bone will not develop bone.

2. One must be just as careful to fasten the graft to the bone as in full thickness graft.

3. The same care must be used in preparing the bed for the reception of the graft as in full thickness graft.

4. It requires a longer time for the graft to become solid.

5. In all bone-graft surgery, one should secure as complete immobilization as possible during the first two months.

6. The thickness and strength of the graft depend upon the amount of weight-bearing that is required.

BIOPSY BY NEEDLE PUNCTURE AND ASPIRATION

By Hayes E. Martin, M.D.
and
Edward B. Ellis
of New York, N. Y.

From the Pathological Laboratory of the Memorial Hospital of New York

This paper is a presentation of technical procedures employed and results attained by securing tissue from suspected neoplasms for histological examination by needle puncture and aspiration.

The use of some form of trocar or needle to obtain tissue from the living subject is not a new procedure. The Mixter punch, a blunt-tipped trocar sharpened with the bevel on the inside, was devised by S. J. Mixter some twenty-five to thirty years ago and has been quite generally employed to obtain specimens of brain tissue. We have been unable to find any published record of its description. Ward,[1] in 1912, suggested needle puncture and aspiration of lymph nodes in the study of lymphoblastomas, and Guthrie,[2] in 1921, reported his observations on the aspiration of nodes in Hodgkin's disease. Goeller,[3] in 1920, devised a trocar with a spiral cutting tip for securing tissue from the prostate. Forkner,[4] in 1927, presented a method by which he obtains a small amount of tissue by the use of a dental broach inserted through an 18-gauge needle, and summarized the results of study of material so obtained by supravital staining.

The Mixter punch, Goeller needle, and the dental broach of Forkner are admirable devices for the purpose intended, but since biopsy by needle puncture is only occasionally indicated, these instruments will commonly be found unavailable. Although the Goeller needle has been employed at Memorial Hospital since its invention, we find, that unless it is made quite heavy, it is too delicate an instrument to keep in repair, and, in any case, it undoubtedly causes more trauma than the method which we present below.

Since 1926, we have employed aspiration with an ordinary 18-gauge needle attached to a Record syringe. This apparatus is always available in any clinic, hospital or office and therefore has the advantage of permitting impromptu and immediate use. We also believe that, with the proper technic and coöperation between the surgeon and pathologist, it is the puncture method most universally applicable. The observations here presented do not include the study of cancer cells from pleural or ascitic fluids, which has already been published[5] by one of us (E).

Indications and Advantages.—The indications for biopsy by needle puncture and aspiration are tumor masses which lie below the surface of normal tissue where surgical exposure is deemed contraindicated for any reason.

The common contraindications to biopsy by surgical exposure may be enumerated as follows: The danger of local or general dissemination of the disease or fungation of tumor tissue through the operative wound, the inter-

ference with subsequent therapeutic surgical procedures, the surgical risk (including hæmorrhage and infection) in obtaining specimens from certain deep-seated masses, and the lack of justification for any procedure involving physical or mental discomfort or expense to the patient, where the information to be gained may be of doubtful value to the patient or of academic interest only.

Biopsy by needle puncture and aspiration has, we believe, none of the above-mentioned disadvantages. The danger of local or general dissemination through the minute break in the tumor capsule produced by an 18-gauge needle is comparatively slight. The procedure has not in our experience

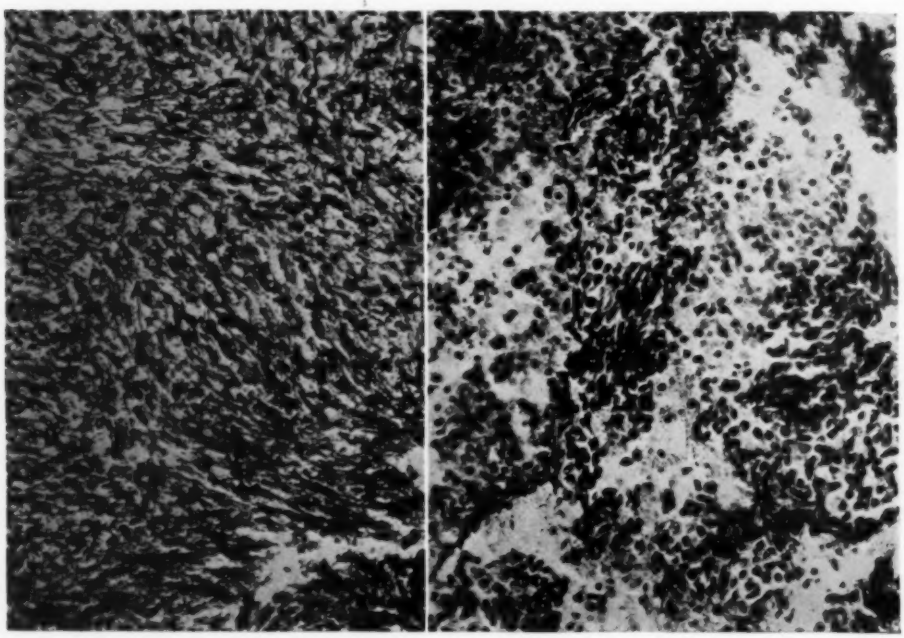

FIG. 1.—Spindle-cell sarcoma of cheek. Paraffin section of aspirated material (Case 1).

FIG. 2.—Carcinoma of lung. Smear of aspirated material (Case 3).

caused sufficient trauma to modify the clinical setting for any subsequent treatment and the surgical risk is negligible, if sterile precautions are observed. We have not considered aspiration of abdominal tumors advisable, but we have several times successfully obtained diagnostic material from masses within the lung, without any untoward symptom either immediate or late.

In a clinic wholly devoted to the treatment of neoplastic diseases, we have several times obtained unsuspected pus or other fluid leading to the diagnosis of a benign lesion.

The procedure is accepted without question by the patient as it does not necessitate hospitalization, elaborate preparation, great discomfort, or more than a few minutes of time. It therefore makes possible histological diagnoses, otherwise either unobtainable or of necessity deferred.

Technic.—The special paraphernalia required is an ordinary 18-gauge needle five to ten centimetres in length (which should be new and sharp) and a twenty cubic centimetre Record syringe. For the preservation of the specimen, glass slides and a specimen bottle with 10 per cent. formalin are needed.

The skin at the site of the intended puncture is painted with iodine and a small area of skin infiltrated with 1 per cent. novocaine. With a bistoury pointed scalpel (No. 11 Bard Parker blade) a stab wound is made through the skin with the instrument held at right angles to the skin surface. This puncture of the skin facilitates insertion of the needle. An 18-gauge needle

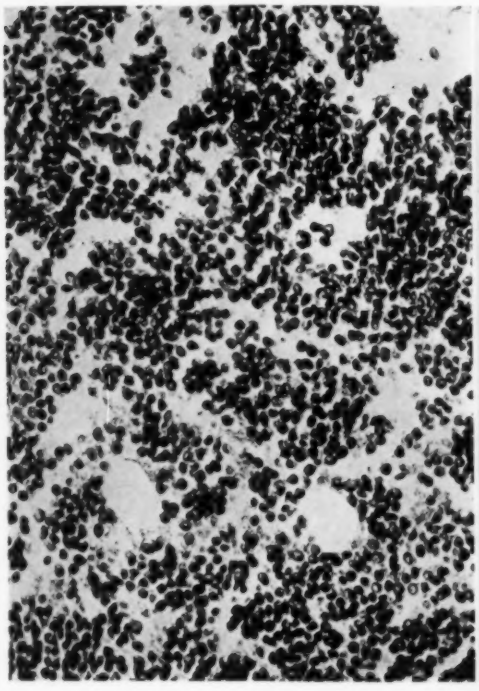

FIG. 3.—Endothelial myeloma of heel. Paraffin section of aspirated material (Case 4).

FIG. 4.—Carcinoma of lung. Smear of aspirated material (Case 8).

attached to a tightly fitting Record syringe is then inserted and advanced slowly through the superficial tissues until the point is felt to enter the suspected neoplastic mass. Guided by palpation with the disengaged hand, it is striking how readily a difference in consistence of the tissues can be felt as the needle enters a mass of neoplasm. When the point of the needle is felt to enter the tumor, the piston of the syringe is partly withdrawn so as to produce a vacuum and the needle slowly advanced one to three centimetres farther, depending on the anatomy and size of the tumor. Maintaining the vacuum, the needle is then withdrawn to the same distance and advanced again. This manipulation may be repeated two or three times at the discretion of the operator, *care being taken to maintain the vaccum when*

the needle is advanced or partly withdrawn. Aspiration with the needle at rest is not sufficient to draw tissue into the needle in most cases. By advancing the needle and aspirating simultaneously, a plug of tissue is both forced and drawn into the needle. Maintaining suction during partial withdrawal detaches the plug of tissue already within the needle. We have found this detail to be very essential. Before the needle is completely withdrawn from the tissue, the piston must be slowly released until the pressure in the needle is equalized, or better still, the syringe detached and the needle withdrawn separately, otherwise the aspirated material will be suddenly drawn and splashed over the interior of the syringe, making its collection difficult. While the needle is being advanced and withdrawn under negative pressure, a small quantity of blood mixed with fragments of tissue may enter the syringe, or a solid cylindrical mass of tissue may appear. In other cases, especially in the firmer masses, the syringe apparently remains empty, but after withdrawal, the needle is usually found to contain a plug of tissue.

After complete withdrawal of the apparatus, the syringe is detached from the needle, filled with air, attached and the contents of the needle slowly and carefully expelled on a glass slide. A small fragment of tissue should be left on the slide for smearing, and the remainder placed in the specimen bottle for fixation and staining by regular methods. If the needle is empty, small masses of tissue can almost always be found mixed with blood in the syringe, and these should, if necessary, be very carefully searched for. One or two of these small masses can readily be fished out upon a glass slide for smearing and immediate staining. In any case where the syringe contains blood or any tissue, formalin from the specimen bottle is poured into the open barrel of the syringe, agitated and returned to the specimen bottle.

Preparation of the Specimen.—In the average case, we have examined the material obtained by two methods: The shorter (a technic devised by one of us [E]) has the advantage of a reading in six to eight minutes and the longer, the advantage of a fixed and cleared preparation.

The Immediate Method.—The fresh tissue fragment on the glass slide is smeared by very firm flat pressure by another glass slide drawn once across. The smeared slide is fixed by heating gently over a gas flame until warm and dry, and is then prepared according to the following technic:

1. Alcohol (95 per cent.)—one minute.
2. Water—one minute.
3. Hæmatoxylin—one minute.
4. Water—one minute.
5. Eosin—one minute.
6. Alcohol (95 per cent.)—one-half minute.
7. Carbol-xylol—one-half minute.
8. Mount with Canada Balsam and cover glass.

Longer Method.—The remainder of the specimen is treated as any small biopsy, being carried through the stages of alcohol fixation and embedding in paraffin, great care being taken to collect and mass every minute particle

of tissue, since a positive diagnosis may often be obtained from the smallest fragment. Absolutely fresh 52°-56° C. paraffin should be used for embedding, and all particles massed together on the block and cooled immediately on ice. Every section cut from the block should be examined for fear that in dealing with such small particles, one might lose the opportunity of making a positive diagnosis. We usually cut six to eight sections and place them on a single slide. These are carefully examined and further sections cut if the first are negative and more material remains on the block.

In case a reading is desired earlier than by our routine laboratory technic, we use the following method of preparation which requires about three hours.

The quick paraffin method:

1. Formalin 10 per cent.—ten minutes.
2. Alcohol 95 per cent.—two changes, ten minutes each.
3. Xylol—two changes, one-half hour each.
4. Paraffin 54° C.—two changes, one-half hour each. (First three steps in incubator 37° C.)
5. Cut and stain.

Interpretation of the Histological Preparation.—The interpretation of the smear, if it is to be of value, requires first of all the experience of a pathologist fully familiar with the field of neoplastic diseases. He must be cognizant of the probable types of tumors peculiar to the region under consideration. He must be aware of the pitfalls introduced into his interpretation by the possible inclusion of crushed normal tissue into his aspiration. He must familiarize himself with the differences in size and relation between the shrunken, fixed tumor cell of the paraffin section and the crushed, loosened, rapidly-fixed tumor cells of aspirated material. He must be associated with a clinician whose clinical interpretation of the facts of the case is accurate and reliable, and he must be capable of intelligently utilizing what may be called his pathological imagination. By the exercise of great care in preparation of both the smear and residue specimen, accurate diagnoses may be made from aspirated material. (Fig. 1.)

The information gleaned from the direct smear is usually sufficient to distinguish between an inflammatory process with leucocytes and lymphocytes predominating, and a malignant tumor with its atypical cells occurring singly or in groups. The paraffin section of the material enables one to classify and often grade the malignant process. Material from lymph nodes, particularly those invaded by epidermoid or squamous carcinoma, often shows liquefied or necrotic material with shadows of epithelial cells, singly or in groups. Careful search of the slide, however, may reveal just one small group of viable cells upon which a definite diagnosis may be made. This type of material often suggests pus, but pus cells are seldom found in the smear, although it may contain many flocculi and shreds of epithelium.

Various types of cells are encountered in the smears: leucocytes, lymphocytes, plasma cells, or swollen endothelial cells which may readily be confused with tumor cells. We search particularly for groups of cells, atypi-

cal in size and shape with definite hyperchromatic nuclei, as it is upon these that the most positive diagnosis of malignant disease can be made. Too much reliance should not be placed upon the direct smear unless one finds a definite group of atypical cells. Any other information should be considered suggestive only, until the paraffin section is secured which can be done in three hours if necessary. In the paraffin section, overlapping of cells and false arrangements are obviated, permitting more accurate classification and grading.

We have been able, however, to make correct diagnoses, as between benign and malignant lesions, in practically all cases and to check the diagnoses in about 60 per cent. of cases by paraffin sections on biopsies obtained by usual methods at a later date during the course of the disease. The smeared preparation should first be examined in its wet state following hæmatoxylin which permits deeper staining if necessary. If the smeared material appears too thick, gentle pressure with another slide may alter the arrangement of packed cells, and afford a better opportunity for staining and clearing. Lymphoid tissue must be left a little longer in alcohol for fixation which enables the cells to take the stain more readily.

When endeavoring to interpret a given smear or section of aspirated material, one must consider the source from which the specimen was obtained. The type of histological structure through which the needle has passed in securing the specimen must be kept in mind. Any structure foreign to this locality encountered in the smear must be carefully noted. Thus if a specimen aspirated from a lymph node in which one would expect lymphocytes or possibly some swollen endothelial cells to predominate, contains instead many epithelial cells, single or grouped, atypical and hyperchromatic, one must admit the probable invasion of this node by an epithelial tumor. If there is central necrosis and liquefaction of a lymph node, the aspirated material contains many loose cells, some necrotic and poorly staining, yet the shadowy outlines of these foreign cells should lead one to search the field for clearer and more typical cells upon which to make a diagnosis. These foci are usually found.

Results of the Method.—During our earlier experience, we were able to secure tissue by aspiration in about 80 per cent. of the cases attempted, the failures usually being in the harder fibrous tumors. With more experience and by more careful attention to the technic of aspiration, we practically always secure tissue. Where tissue was obtained, we have been able to distinguish between its malignant and benign nature in all cases and as our pathological staff becomes more familiar with the examination of tissue smears and fixed aspirated material, we are more often able to definitely classify the tumor process.

In Table I are listed sixty-five cases of neoplastic disease in which the diagnosis has been made by this method. In about 60 per cent. of the cases in this series the aspiration diagnoses have been checked and confirmed by histological sections, obtained and prepared in the usual manner. We have

TABLE I

Case No.	Clinical diagnosis	Site of aspiration	Histological diagnosis of aspirated material
1.	Tumor of cheek	Primary tumor through cheek	Spindle-cell sarcoma*
2.	Mediastinal tumor perforating sternum	Through skin over sternum	Solid cellular malignant tumor without definite epithelial character resembling lymphosarcoma or thymic tumor
3.	Tumor of lung	Lung tumor through posterior chest wall	Epidermoid carcinoma
4.	Tumor of heel	Heel	Endothelial myeloma
5.	Tumor of cheek	Cheek	Small-celled alveolar carcinoma,* salivary gland type
6.	Carcinoma (?) antrum	Antrum through cheek	Glandular carcinoma,* adenoma malignum
7.	Carcinoma (?) antrum	Antrum through cheek	Malignant epithelial tumor, probably transitional cell carcinoma*
8.	Tumor of lung	Lung tumor through posterior chest wall	Epidermoid carcinoma
9.	Carcinoma of tongue	Questionable metastatic neck node	Squamous carcinoma*
10.	Carcinoma (?) of thyroid or larynx	Tumor at anterior base of neck	Epidermoid carcinoma, probably from larynx
11.	Carcinoma (?) of thyroid or larynx	Tumor at anterior base of neck	Epidermoid carcinoma
12.	Sarcoma (?) of mandible	Primary tumor through alveolus	Chondrosarcoma*
13.	Adenoid cystic epithelioma of scalp	Metastasis in ilium at sacro - iliac joint	Adenoid cystic epithelioma*
14.	Post-operative tumor of submaxillary gland	Recurrence in submaxillary region	Adenoma malignum*
15.	Tumor of breast	Breast tumor	Loose malignant epithelial tumor,* no definite structure apparent
16.	Tumor of breast	Breast tumor	Alveolar carcinoma*
17.	Tumor of breast	Breast tumor	Malignant epithelial tumor consistent with breast carcinoma*
18.	Tumor of breast	Breast tumor	Malignant epithelial tumor consistent with breast carcinoma*
19.	Carcinoma (?) of larynx	Neck node	Squamous carcinoma
20.	Tumor of breast	Breast tumor	Malignant epithelial tumor consistent with breast carcinoma *
21.	Carcinoma (?) of sigmoid	Subcutaneous metastasis of chest wall	Adenocarcinoma*

* Indicates that the aspiration diagnosis was confirmed by paraffin section on larger biopsy obtained by the usual methods.

TABLE I—*Continued*

Case No.	Clinical diagnosis	Site of aspiration	Histological diagnosis of aspirated material
22.	Tumor of neck	Neck mass	Hodgkin's disease
23.	Cystic tumor of jaw	Jaw tumor	Malignant epithelial tumor*
24.	Carcinoma (?) of larynx	Neck node	Squamous carcinoma
25.	Tumor of neck	Neck mass	Squamous carcinoma
26.	Carcinoma of tongue	Questionable neck node	Squamous carcinoma*
27.	Carcinoma (?) of antrum	Antrum through cheek	Squamous carcinoma*
28.	Tumor of neck	Neck node	Epidermoid carcinoma*
29.	Tumor of soft palate	Soft palate	Mixed tumor, salivary gland type*
30.	Carcinoma of floor of mouth	Submental node	Epidermoid carcinoma*
31.	Carcinoma of tongue	Neck node	Epidermoid carcinoma*
32.	Cervical adenopathy	Neck node	Transitional-cell carcinoma
33.	Carcinoma of tongue	Neck node	Epidermoid carcinoma*
34.	Carcinoma (?) of tonsil	Neck node	Malignant tumor, either a lymphoepithelioma or lymphosarcoma
35.	Cervical adenopathy	Neck node	Malignant tumor
36.	Carcinoma of cheek	Neck node	Epidermoid carcinoma*
37.	Cervical adenopathy	Neck node	Anaplastic epidermoid carcinoma
38.	Sarcoma (?) of humerus	Tumor of humerus	Osteogenic sarcoma*
39.	Carcinoma of thyroid	Neck node	Clusters of tumor cells
40.	Carcinoma of face	Mass over parotid gland	Squamous carcinoma*
41.	Carcinoma of œsophagus	Neck node	Degenerative squamous carcinoma*
42.	Carcinoma of parotid gland	Neck node	Squamous carcinoma*
43.	Carcinoma of tongue	Neck node	Epidermoid carcinoma*
44.	Sarcoma (?) of scapula	Tumor of scapula	Primary bone tumor with giant cells of type found in benign giant-cell tumor, though this is not sufficient to exclude malignant bone tumor
45.	Carcinoma (?) of submaxillary salivary gland	Submaxillary tumor	Tumor cells present, probably epidermoid carcinoma. (Later pathology after removal, mixed tumor, salivary gland type)

* Indicates that the aspiration diagnosis was confirmed by paraffin section on larger biopsy obtained by the usual methods.

TABLE I—*Continued*

Case No.	Clinical diagnosis	Site of aspiration	Histological diagnosis of aspirated material
46.	Epulis (?)	Tumor of alveolus	Giant-cell epulis*
47.	Carcinoma of tongue	Neck node	Liquefied squamous carcinoma*
48.	Carcinoma (?) of thyroid	Neck mass	Numerous large spindle tumor cells, some with mitoses. Probably large spindle-cell thyroid carcinoma
49.	Transitional cell carcinoma of tonsil	Mass in scalp	Tumor cells present—type not determined.* (Specimen from tonsil—transitional-cell carcinoma)
50.	Lympho - epithelioma of tonsil	Diffuse swelling of forearm	Very cellular epithelial tumor, suggesting transitional-cell carcinoma*
51.	Lymphosarcoma (?) of neck	Neck node	Cellular epidermoid carcinoma
52.	Carcinoma (?) of antrum	Antrum through anterior wall	Schneiderian carcinoma*
53.	Cervical adenopathy	Neck mass	Squamous carcinoma
54.	Sarcoma (?) of humerus	Tumor of arm	Spindle-cell sarcoma, probably osteogenic
55.	Carcinoma (?) of prostate	Prostate through perineum	Carcinoma
56.	Carcinoma (?) of thyroid	Thyroid tumor	Malignant tumor, type undetermined
57.	Carcinoma of soft palate	Neck node	Transitional-cell carcinoma*
58.	Carcinoma of tongue	Neck node	Squamous carcinoma
59.	Carcinoma of floor of mouth	Neck node	Epidermoid carcinoma*
60.	Tumor of anterior chest wall	Chest wall tumor	Tumor cells in sheets are spindle and polyhedral, would consider carcinoma—possible thymic, thyroid or bronchogenetic
61.	Tumor of thigh or femur	Thigh	Multinucleated tumor giant cells. Sarcomatous tumor probably neurogenic or myogenic
62.	Tumor of pelvis	Pelvic tumor	Masses of atypical cartilage cells—either chondroma or chondrosarcoma
63.	Cervical adenopathy	Neck node	Solid sheets of large lymphoid cells, consistent with reticulum-cell lymphosarcoma
64.	Tumor of breast	Breast tumor	Large number of spindle and polyhedral cells with atypical mitoses—sarcoma
65.	Tumor of thigh	Thigh tumor	Spindle-cell sarcoma—neurogenic

kept no definite record of the instances in which normal tissue, pus, or other fluid has led to an eventual diagnosis of a benign lesion. Obviously the

* Indicates that the aspiration diagnosis was confirmed by paraffin section on larger biopsy obtained by the usual methods.

aspiration of normal tissue may not be considered alone as conclusive evidence of a benign process.

The actual value of this method of biopsy in selected cases depends upon the fact that diagnoses can be made without loss of time and in instances where there are definite contraindications or obstacles to securing tissue by any other method. If in any case tissue can readily and safely be secured in larger amounts by any other procedure, there is no advantage in aspiration. An analysis of the cases in Table I will illustrate indications and advantages of the method in our series.

Nodes of the Neck.—In almost half of the cases in our series, the aspiration was done on neck nodes or masses. The indications and value of this

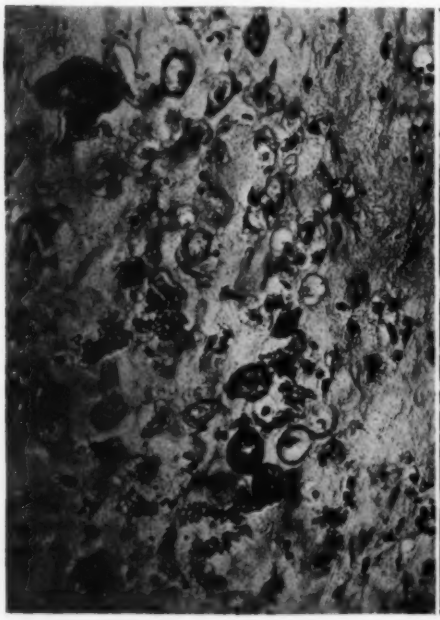

FIG. 5.—Chondrosarcoma of mandible. Smear of aspirated material (Case 12).

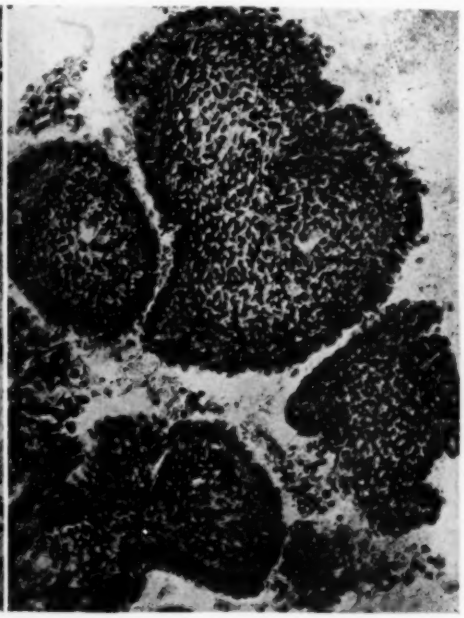

FIG. 6.—Adenoma malignum of metastatic neck node. Paraffin section of aspirated material (Case 14).

method of biopsy in neck nodes is illustrated by the citation of a few of these cases.

In Cases 22 and 25 there were firm solid masses in the neck without any other definite clinical or laboratory evidence of a primary or constitutional disease. Aspiration quickly established the diagnoses as Hodgkin's disease and squamous carcinoma respectively.

Cases 10 and 11 presented indurated fixed masses at the anterior base of the neck with moderate dyspnœa. Laryngeal examinations showed infiltration and pressure on the larynx, but no ulceration. The diagnosis lay between carcinoma of the thyroid and carcinoma of the larynx. Aspiration of the neck mass revealed squamous carcinoma in each case, establishing the larynx as the original site of the disease.

Cases 19 and 24 presented typical clinical pictures of moderately advanced carcinoma of the larynx. Biopsies taken, twice in each case, from ulcerating and granular tissue within the larynx, showed simply granulation tissue. Neck nodes in each case were aspirated and squamous carcinoma found, establishing the diagnosis for a prognosis and for completion of the records. In Case 2 a diagnosis of a malignant process was obtained for record.

In Cases 9 and 26 the diagnoses had been made by biopsies from the primary lesions, but in subsequently developing neck nodes, the question of their metastatic or benign nature arose in determining treatment. In each of these cases, aspiration definitely settled their metastatic character and

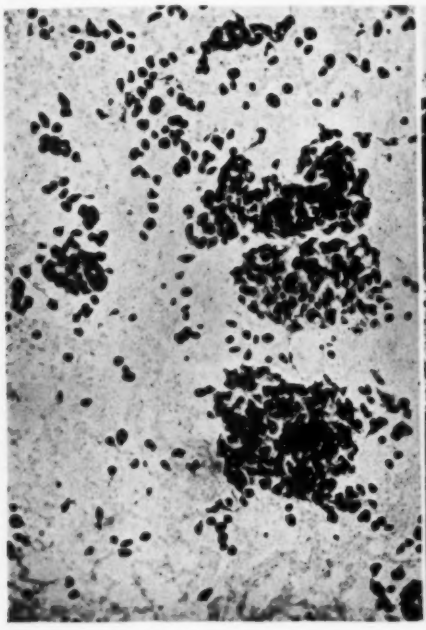

FIG. 7.—Carcinoma of breast. Smear of aspirated material (Case 15).

FIG. 8.—Epidermoid carcinoma of metastatic neck node. Smear of aspirated material (Case 24).

appropriate measures were taken. Case 14 came to Memorial Hospital with a local recurrence about eight months after operative removal of a submaxillary mass. We were unable to secure a pathological report from the operating surgeon, but aspiration showed adenoma malignum.

Intra-Oral Tumors.—In Cases 1, 23, 29, and 46 there were non-ulcerating tumors of the cheek and jaw in which incision carried with it the danger of fungation of the tumor. By aspiration we were able to diagnose them as spindle-cell sarcoma, parotid tumor, mixed tumor of salivary gland type, and epulis, respectively.

Tumors of the Antrum.—Unless the disease has perforated the hard palate or into the nasal cavity, biopsy must usually await antrotomy. In Cases 6, 7, 27, and 52 aspiration was done through the cheek and partly

eroded bone of the anterior antral wall. A diagnosis of carcinoma was made in each case without waiting for operation.

Tumors of the Lung.—In Cases 3 and 8, X-rays showed a mass within the parenchyma of the upper lobe of the lung. Bronchoscopic examinations were negative and offered no opportunity for biopsy. After a careful study of stereo-röntgenograms, a needle was inserted through the chest wall and material aspirated upon which a diagnosis of carcinoma was made.

Tumors of the Breast.—In Cases 15, 16, 17, 18, and 20 there was a real question in the mind of the surgeon as to whether he was dealing with benign or malignant tumors. This question might eventually have been decided during treatment at operation, but we believe that it has been of definite value, both to the patient and surgeon, to have an immediate definite diagnosis in order to plan and expedite both irradiation and possible surgery. In Case 64, there was a large non-ulcerating tumor of the breast in which aspiration made possible the rather rare diagnosis of sarcoma.

The danger of favoring metastases by the manipulation of aspiration in breast tumors is, of course, to be seriously considered but, where the diagnosis is much in doubt, it is ordinarily settled by surgical exposure and frozen section which would undoubtedly be a far greater factor in dissemination than simple puncture and aspiration.

Sarcoma of Bone.—In Cases 12, 38, 44, 54, and 62 diagnoses of various types of bone sarcoma were made from aspirated material. In two of these cases, the diagnoses were checked later by histological section of post-operative material and found correct. The danger of fungation of bone sarcoma through the operative incision is wholly eliminated by aspiration and it seems to us that the chances of general dissemination are slight. Coley [6] admits the hazards of surgical biopsy, but insists that it should be done in all cases of suspected giant-cell tumors of bone, in which conservative therapeutic measures (radiation or curettage) are to be used. He arrives at these conclusions after an analysis of thirty cases of supposed giant-cell tumors in which there was an error of 25 per cent. in röntgenray diagnoses in various clinics. His views are opposed by those who maintain that the dangers of surgical biopsy outweigh the advantages, should the case be one of malignant bone tumor rather than a benign giant-cell type. It seems to us that both sides of the question might be answered by an aspiration diagnosis.

Miscellaneous Tumors.—In Cases 2, 4, 5, 21, 28, 32, 34, and 45, the nature of various tumors, primary or metastatic, was determined without danger of fungation through an incision. In this group the wide range of usefulness of aspiration in the study of malignant disease is again illustrated. Quite often the knowledge of an individual case must remain incomplete because further investigation would cause unjustifiable suffering or other unfavorable consequences. In certain instances these investigations may not benefit the patient, but may be of great interest in the general study of the disease.

The importance of histological diagnosis in the treatment of neoplastic

disease needs no emphasis. In some clinics it is mandatory before treatment by radiation. Biopsy by surgical exposure is too often extremely ill-advised when casually performed by a surgeon who contemplates no further treatment, and it should be severely condemned when done in this manner without careful consideration and definite purpose.

Biopsy by aspiration has, we feel, few, if any, disadvantages to the patient from the surgical standpoint. The interpretation of the histological picture (especially of the smears) requires both an experienced and sympathetic pathologist. Undoubtedly, larger specimens uniformly fixed and stained offer more satisfactory material upon which to render a definite opinion, but such a preparation can too often be obtained only at considerable disadvantage to the patient or too late to be of any particular value in outlining treatment. A post-mortem diagnosis never benefits the one most concerned, the donor of the specimen.

We do not advocate this method of biopsy in any case where larger specimens of tissue can be readily and safely secured by any other method. The chief disadvantage of biopsy by aspiration is that one diameter of the specimen is very small—the same as the bore of the needle. In such a small specimen the characteristic cell arrangement may be difficult to determine as, for instance, in glandular carcinoma. In a smeared specimen it is usually lost entirely. While the lack of definite cell arrangement in smears or very small fragments often prevents accurate classification of the lesion, one is still able to definitely determine whether such tissue is malignant or benign. The accurate classification of tissue specimens is quite often impossible with frozen sections and when one considers the difficulty experienced with frozen sections, often too thick or poorly stained, and compares the necessary time and equipment required for that method with the rapidity and ease of preparation of smears from aspirated material, it might well become the method of choice when fortified by paraffin section of a portion of the same material.

We are indebted to Doctor Ewing and Doctor Stewart for many helpful suggestions and for the interpretation of the histological findings.

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TRAUMATIC LESIONS OF THE BRACHIAL PLEXUS*

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In presenting these cases of traumatic lesions of the brachial plexus from the surgical clinics of J. Chalmers DaCosta, of the Jefferson Medical College, one is impressed with the improvement since the World War in the technic of the operative treatment of peripheral nerve lesions. The improvement in the treatment of these cases is not only because of the immense experience gained at the operating table during and subsequent to the War, but is augmented by a vast amount of scientific and experimental work. Sheehy and Tilney (1915) wrote on the development of the peripheral nerve. Heinemann (1916) disputed the accepted views of the internal topography of peripheral nerves. His publication (Arch. f. klin. Chir., vol. cviii, p. 107, 1916) definitely disproved the old and accepted view of the existence of definite nerve paths from the plexus to the periphery by showing that in the musculo-spiral, median and ulnar nerves there were many internal nerve plexi rather than one continuous pathway. The presence of these peripheral plexi no doubt explains the remarkably rapid improvement in Case II of this series. A man who had had a total motor and sensory paralysis of the brachial plexus of four months' duration regained muscle tone in the flexors of his forearm two weeks after operation. To use his own expression, "the softness of the flesh disappeared and it became firm." It would seem almost an impossibility for a continuous pathway to be reëstablished within this short period, a view held by Stoeffel (Zts. fur Orthop. Chir. Bd., vol. xxv, p. 505, 1910). But it would agree with Compton (Journ. Anat. and Physiol., vol. li, p. 103, 1916–1917) who verified the observations of Heinemann and added that one of the functions of the plexpleni in the nerve was to supply several routes to each muscle for the impulse to reach it. The function of the nerve plexpleni within the peripheral nerves would explain the early development of muscle tone in Case II, above cited, and would further lead us to believe that peripheral nerve plexi are more resistant to degeneration than is generally believed. This fact is verified by our observations in Case VI. The patient was not operated upon until four years after the injury. Subsequently, he had return of sensation down to the elbow and some return of power in some of the muscles of the shoulder girdle. A. P. Dustin (Ambulance de L'Oceon, p. 135, July, 1918) accepted Heinemann's and Compton's views on the internal topography of the peripheral nerves and wrote: "It is possible to establish as a Principle, that the identical arrangement is never found at the same level in two different individuals and that it is impossible to conceive of a fundamental systematization of a nerve

* Read before the Philadelphia Academy of Surgery, April 7, 1930.

having funiculi as its anatomical basis." With these fundamental principles on the internal topography of peripheral nerves and the reëstablishment of impulses in divided peripheral nerves, surgery of the peripheral nerves was placed on a solid operative basis.

Let us now consider the etiology of brachial plexus—paralysis—overstretching and division of one or several of the component parts of the brachial plexus, due to a force which increases the acromiomastoid line, thereby forcing the head and shoulders apart. Were the overstretching and rupture of the nerve structure the only pathologic process present in these individuals, the conservative plan of treatment could be used more frequently and with more success, but, the presence of intraneural and extraneural hæmorrhage must be considered. Stookey, p. 25, Saunders and Co., 1926, shows a cross section of a peripheral nerve. A glance will show how well supplied the peripheral nerves are with blood, and no slight stretch of the imagination is required to envision the damage that can be done by free hæmorrhage within the sheath.

Case II is a striking example of the damage done by hæmorrhage within the nerves. There was complete paralysis of the brachial plexus below the roots, manifested by a total palsy of all the muscles of the shoulder and arm.

The early opening of the sheath before fibrosis takes place would anticipate much subsequent damage to the plexus.

If the conductivity of the nerve is interrupted by laceration, vulsion or gun-shot wound (the local pathology), what happens to the distal portion of the nerve? This was clearly explained by Waller in 1852, at which time he demonstrated that secondary degeneration took place when the periphery was severed from the ganglion cell. This is known as Wallerian degeneration. Stookey states: "Within twenty-four to forty-eight hours after an injury to a peripheral nerve the muscles supplied by the nerve will respond to mechanical and electrical stimulation. After four days, change in the myelin sheath is observed, and this is followed by segmentation of the myelin sheath and fragmentation of the neuraxis. At the end of the first week after the injury which causes degeneration, nearly all of the nerve fibres of the distal portion of the nerve present varying evidence of degeneration. The degenerative process is progressive up to the end of the third week, then degeneration reaches a resting stage in the form of syncytial, nucleated, protoplasmic bands, the product of hyperplasia, of neurilemma cells and the proliferation of their nuclei within the old neurilemma sheath." This constitutes a resting stage of degeneration in the peripheral segment and remains practically unaltered for weeks and months and may be indefinitely, as exemplified by one of our patients who was operated upon four years after he developed a complete paralysis of the brachial plexus. At the time of operation he had reactions of degeneration of all of the muscles supplied by the brachial plexus. This, of course, was to be expected as reactions of degeneration may be determined six

weeks after division of the nerves, if the studies are carried out by a competent man.

If the old theory of complete degeneration of the nerves were true and that restoration of function had to be reëstablished along a single neuraxis, it would seem impossible that any return of function could take place after a lapse of years, but with the understanding that the nerve reaches a resting stage of degeneration, one is justified in operating upon patients with divided nerves even a year after the injury.

Diagnosis.—Some times it is questionable whether the brachial plexus is injured above or below the clavicle. This is especially true in gun-shot wounds about the neck and chest and in cervical spinal column injuries. Three of our patients presented this problem. If one considers that the muscles of the shoulder girdle are supplied by the nerves coming directly from the roots or at their primary subdivision then paralysis of one or all of these muscles means a supraclavicular injury to the plexus; on the other hand, if all the muscles of the shoulder girdle are functioning normally the traumatism is below the clavicle.

While this method of diagnosis of the lesion is helpful, it is not sufficiently accurate to definitely localize the divided nerves. This information must be definite before the incision is made. A mental picture of the plexus, together with the site of the lesion, is most essential in making the correct diagnosis.

"The nerve root is a morphological unit; the nerve trunk a physiological unit." (Stookey.) Stimulation of a root produces contraction of both flexor and extensor muscles; therefore, division of a root produces paralysis of flexors and extensors. Stimulation of a nerve trunk produces flexion or extension and never both; likewise, division of a nerve trunk never produces paralysis of flexors and extensors. It follows that if there be both flexor and extensor paralysis, and the shoulder girdle muscles are functioning normally, the lesion is in the secondary cords. There is some variation in the formation of the brachial plexus in different individuals, especially between the fourth and fifth cervical roots and the first dorsal root. This variation is determined only by exposure of the plexus.

The brachial plexus is divided into nerve roots, two primary cords, three secondary cords, and their trunks and branches. The ventral and dorsal roots of a spinal nerve unite within the intervertebral foramen. Consequently, an evulsion involving the roots of the brachial plexus is often associated with a tear of the dura and the escape of cerebrospinal fluid. This pathology was found in Case I of this series. It is seldom that all the roots are divided. There is usually a combination of root and primary cord lesion.

Let us see what nerves have their origin in the roots of the brachial plexus—the dorsalis scapulæ, which supplies rhomboideii and levator anguli scapulæ; the long thoracic nerve which supplies the serratus magnus; the

phrenic nerve which is derived from the fourth and fifth root in the prefix type of plexus and from the fifth root alone in the postfixed type of plexus. Paralysis of any or all of the muscles supplied by these nerves means root pathology. The oculopupillary fibre of the cervical sympathetic is also a key to involvement of the cervical roots. These fibres supply the dilator pupillæ, the non-striated part of the levator palpebræ superioris and the orbital muscles of Muller, a small bundle of non-striated muscle which lies behind the globe of the eye. The pupillary dilator fibres arise from the cortical centre in the frontal lobe, pass along the brain stem to the pupil dilating centre in the medulla. They then descend in the lateral column of the spinal cord to the ciliospinal centres in the lower cervical region, emerging from the cord as pre-ganglionic fibres through the anterior roots of the first and second thoracic segment, and enter the inferior cervical ganglion of the cervical sympathetic by the white rami communicans. They then ascend as post-ganglionic fibres behind the carotid sheath in the neck to the gasserian ganglion and pass along the ophthalmic division of the fifth nerve as the long ciliary nerve to the pupil. When this pathway is destroyed as the result of an injury in the neck, there is ptosis of the eyelid, contraction of the pupil on the side of the paralysis, due to paralysis of the dilator pupillæ, and the eye is slightly sunken—"enophthalmos." Two patients of this series presented this picture.

While it is true there is no definite communication between the brachial plexus and the ciliary spinal reflex, the abolishment of the ciliary spinal reflex should lead us to make a careful investigation, to determine the presence or abscence of an injury to the upper roots of the brachial plexus.

The spinal roots divide to form the inner, outer and posterior cords of the brachial plexus. At the junction of the division of the fifth root, the suprascapular nerve takes its origin and consequently a paralysis of the suprascapular nerve would definitely isolate the site of the pathology. The suprascapular nerve supplies the supra- and infra-spinati muscles. We, therefore, conclude that in injuries to the brachial plexus, above the clavicle, there must be paralysis of some or all of the muscles of the shoulder girdle, the rhomboideii or levator anguli scapulæ, serratus magnus, supra-spinatus and infra-spinatus and sub-clavius muscles; whereas, in an injury below the clavicle, all the muscles of the scapula function normally.

There are three classical types of brachial paralysis: the upper cervical or Duchenne-Erb, the middle and the lower cervical. In three cases of our series, in which extensive paralysis was present, it was observed at operation that the primary rupture was not the sole cause of the paralysis; fibrosis and hæmorrhage were responsible for much of the damage—an observation which militates against the conservative plan of treatment.

Treatment.—The treatment of brachial plexus palsy, whether due to birth injury or to traumatism, is conservative and operative. For the conservative plan we can say little to encourage the use of this plan in traumatic cases.

It does not correct the primary division of the nerve structures, and it does not prevent the secondary inflammatory fibrosis from taking place. Why hesitate when the simple operation of neurotomy will restore the function of many muscles by preventing inflammatory fibrosis and proper suturing, if done promptly, will restore a useful if not a perfect arm.

The technic of the operative plan of treatment may be found in detail in Stookey's book.

CONCLUSIONS

1. The distal portion of a traumatized or divided peripheral nerve is very resistant to degeneration.

2. Return of function may be obtained months and years after the operation.

3. Definite localization of the site of traumatism must be known. Direct force will often injure the lamina or the body of the cervical vertebræ, causing damage to the spinal cord, but does not traumatize the roots, trunks or branches, causing paralysis of the arms, which simulates avulsion of the plexus. These cases improve under the conservative plan of treatment.

4. Where the injury causes wide separation of the acromiomastoid line, we are dealing with local pathology in the plexus which requires surgical intervention.

5. Early surgical intervention prevents fibrosis and years of convalescence.

CASE REPORTS

CASE I.—*Traumatic Avulsion of Brachial Plexus.*—G. L., colored male, aged twenty-three years, M-6345, admitted to Jefferson Hospital December 19, 1924, with complete loss of power and sensation in left arm; pain and stiffness in neck.

Present Illness.—One week before admission to the hospital the patient was struck by some scaffolding which had fallen several stories. It struck him on the back of the head, neck and left shoulder. He awoke in another hospital three hours later and was unable to move the left arm or feel anything in it. For three days he was unable to see with the left eye. On the fourth and fifth days he bled a small amount from the left ear. He complained of pain and stiffness in the neck and was unable to flex his head forward. There was some weakness of the left leg which was not present on his admission to the Jefferson Hospital.

Physical Examination.—Head, scalp, eyes, ears and *nose* negative. *Face.*—Slight left-sided weakness. *Neck.*—No pulsations or enlarged thyroid present. Posterior cervical glands enlarged. Fifth and sixth cervical and first dorsal spines are tender. Rotation of neck painful to some extent. Flexion of head and neck limited. *Thorax.*—Expansion free and equal, though he complains of pain around the left clavicle on inspiration. Percussion note clear throughout. Breath sounds clear, vesicular. No râles. Practically the whole of the thorax is tender on pressure. No fracture of ribs demonstrable.

Extremities.—Legs.—Left knee slight contusion. No evidence of other injury. Power in left leg slightly decreased. Reflexes on both sides diminished. No Babinski or clonus. Sensation unimpaired.

Arms and Shoulders.—Right side, reflex normal. Slight tremor of fingers. Power and sensation unimpaired. *Left* side, paralyzed and anæsthetic; extending up whole arm

to line of axilla. Tenderness over scapula muscles and extreme tenderness in axilla and above clavicle. Reflex absent. Paralysis of all of the muscles of the shoulder girdle.

X-ray Report December 20, 1924.—No evidence of fracture of the lumbar column or dorsal column. First rib on the left side may be disarticulated with the vertebræ, if the injury was in that region. No definite X-ray evidence of fractured skull. Antero-posterior view shows no fracture of cervical vertebræ.

Examination by Doctor Gilpin, December 26, 1924.—Reflexes are diminished but not absent in left forearm. Cannot explain loss of sensation and the presence of reflexes on organic basis. Will see patient again. Electrical reaction will be of great aid in diagnosis.

January 2, 1925.—Patient has loss of reflexes in paralyzed arm. No return of sensation over entire arm and hand. Very tender to pressure over brachial plexus.

January 9, 1925.—No return of sensations since last examination. Muscle atrophy taking place.

February 1, 1925.—Reaction of degeneration present.

Operation, February 14, 1925.—Incision exposing the roots and brachial plexus. The sheath of plexus opened. At the outlet of the spinal roots of the fifth, sixth and seventh cervical nerves, there was a definite cystic area; this was opened and there was an escape of cerebrospinal fluid. An attempt was made to find the proximal ends, but this was unsuccessful. The eighth cervical and the first dorsal roots were intact but the remainder of the plexus was a mass of inflammatory tissue. Neurotomy was done on all of the roots and trunks above and below the clavicle (which was divided at operation). The distal ends of the outer cord were implanted into the inner cord. Incision was closed with drainage. Fluid sent to laboratory (cerebrospinal).

Progress.—Patient made an uneventful operative recovery. Sensation returned in the arm down to the hand in the course of three months. There was some return of power to the muscles of the shoulder girdle but no return of power in any of the muscles of the arm, forearm or hand. *Discharged* March 14, 1925. Slightly improved.

Comment.—Patient was treated for one week in another hospital. He was then discharged with the diagnosis of hysteria. Too much time was wasted in waiting between the injury and the operation. Recall, Doctor Gilpin reported that reflexes were present in the forearm two weeks after the injury, but reflexes were absent at the time of operation, consequently, inflammatory changes, as a result of hæmorrhage and fibrosis, destroyed the remaining intact nerves.

The arm was amputated nine months after primary operation to settle a law suit. He now has good use of the shoulder girdle muscles (January, 1930).

Case II.—*Brachial Palsy.* H. S., white male, aged forty-two years, H–10356, admitted to Jefferson Hospital April 1, 1929.

Chief Complaint.—Loss of use of right arm. Tingling sensation in fingers and arm.

Present Illness.—Patient states that on March 24, one week before admission to the hospital, while crossing the street, he was struck a glancing blow by an automobile. The impact of the blow knocked him down but not unconscious. He got up, brushed his clothes and proceeded on home and went to bed. On awakening about noon he noticed that he had been sleeping on his right arm. The arm felt numb and heavy and he was unable to use it. He noticed there was some slight pain in the base of the neck on the right side. He called his physician that afternoon who referred him to the hospital. Patient went to a hospital where he had electrical and heat therapy but without improvement. During the past week the sensory sensations have returned somewhat, but there has been no return of motor power.

Physical Examination.—Neck.—There is a swelling at the base of the neck on the right side, extending posteriorly. *Extremities.*—Reflexes normal in all but right arm. No clubbing, no œdema. Right upper extremity is flaccid. Patient has no power in

muscles below shoulder. Some sensation is present down the entire arm and hand, except on the finger-tips. Reflexes absent.

X-ray Report, April 3, 1929.—No X-ray evidence of abnormality of any of the bones of the right shoulder and there is no evidence of abnormality of any of the lower four cervical vertebræ on the antero-posterior exposures. No satisfactory film of the dorsal bodies. There are numerous calcified tubercles in the upper portion of the right lung.

Operation, April 13, 1929.—The sheath of the brachial plexus was opened, the plexus exposed from the roots to the clavicle. The nerves were not divided but were hard and fibrous. Definite hæmorrhage was present in the sheath. *Procedure.*—Each trunk and branch of the plexus was inspected and found to be fibrous. In some of the trunks there was definite evidence of recent hæmorrhage. Neurotomy was done on almost every nerve trunk and branches above the clavicle. The incision was closed without drainage.

Progress.—April 14, 1929.—Twenty-four hours after the operation, the patient was

FIG. 1.—Case II. Shows return of function following neurotomy of the roots and trunks of the brachial plexus above the clavicle. (The paralysis was due to intra-neural and extra-neural hæmorrhage.

able to move the fingers with the exception of the thumb. One can feel an attempt at flexion of the tendons of the arm.

April 15, 1929.—Patient was able to feebly abduct and adduct thumb. There is motion in all of the fingers. He complained of excruciating pain in the arm, for which morphine was required.

June 7, 1929.—Discharged, improved.

January, 1930.—There is some limitation of flexion and extension of the fingers. He cannot entirely extend the wrist.

Comment.—Early operative intervention was followed by an almost unbelievable return of motion in the paralyzed arm (twenty-four hours).

CASE III.—*Brachial Palsy, Left Arm.* F. H., white male, aged nine years, R–3073, admitted to the Jefferson Hospital August 24, 1928, four years after the injury.

Chief Complaint.—Complete motor paralysis of left hand, arm and muscles of the shoulder girdle. Total loss of sensation below the axillary fold.

Present Illness.—Four years before admission to Jefferson Hospital he was struck by an automobile.

Examination of Left Arm.—Complete palsy of all of the muscles of the left upper extremity. There is a suggestion of slight rotation (internal) of the head of the humerus. Sensation is lost below the upper third of the arm (humerus) on the outer side and below the lower one-third of the inner side. Sensation is present above these regions.

The muscles over the scapula, supra-and infra-spinatus and teres minor are atrophied and the serratus magnus left and pectoralis major left are also atrophied so that the left chest is flattened. He has no sensation to heat, cold or pin over left arm except in upper third internally. Sensation is not absent over the scapula area.

September 30, 1928.—Examination by Doctor Rugh. This case presents two phases, one, a possible anterior poliomyelitis with loss of sensation (a rare complication) and, second, traumatic avulsion of nerve trunks, nerve roots or destruction of nerve cells.

October 5, 1928.—Examination by Doctor Strecker. Traumatic brachial paralysis. Reaction degeneration is complete in left arm.

October 9, 1928.—Examination of eye grounds under homatropine by Doctor Heed. R. E., media clear, disc slight pallor, margins not sharp, depression but no lamina. Capillaries rather over-full. Retinal vessels appear healthy. No gross lesion of retina or choroid. L. E. similar. Diagnosis.—Suggestive of an old neuritis of both eyes. No pressure signs at present.

October 16, 1928.—Examination of pupils by Doctor Heed. R. E., 7 millimetres, L. E., 5 millimetres. Both react promptly to light and convergence. The inequality I believe is due to irritation of the cervical sympathetic.

Operation December 22, 1928.—Incision exposing the brachial plexus, the sheath opened. A definite hæmorrhagic cyst was present involving all of the cords of the plexus. The outer cord was avulsed at the roots. After careful dissection with a sharp knife some of the fibrosi were removed, the cords and nerves were hard, firm and shrunken in size. The end of the divided outer cord was freshened and implanted into the posterior cord and sutured with catgut. Neurotomy was performed on trunks and branches of the plexus. The incision was closed without drainage.

Progress.—The child remained in the hospital for a number of months and was discharged unimproved. He was followed in the out-patient department for six additional months. There was no evidence of improvement in muscular power of the arm; although he had attacks of pain which reached the palm of the hand. No further progress, if this one slight manifestation could be considered progress. We advised the mother of the child to have the paralyzed arm amputated. This she refused. In January, 1930, there were no trophic lesions present. He was able to shrug his left shoulder and pull his arm toward the chest. He had more frequent attacks of pain down the arm to the palm of the hand. There was no other improvement in the arm.

Comment.—The records of the first hospital where the child was taken state: "Patient has about one-third normal motion of the injured arm. There is slight sensation throughout the entire arm." Four years after this, Doctor Strecker reports a total brachial plexus paralysis. This is something for the advocates of the conservative plan of treatment to think about. Again recall the findings at the operation, a hæmorrhagic cyst and a divided outer cord, both conditions amenable to operative procedure. Compare the results in this case with those of Case II, in which case there was sensation in the arm but no muscle power, yet, the case report of No. II shows at operation, done two weeks after the injury, "hæmorrhage in the plexus." The patient was able to move his fingers barely four hours after the operation. There is no doubt, as you gentlemen can observe, that this child operated upon four years after the injury, can shrug his left shoulder and has some power to abduct the arm. Previous to the operation he was unable to perform either of these movements in Dr. J. Chalmers DaCosta's Clinic or when Doctor Rugh presented him before the Orthopedic Society.

CASE IV.—*Avulsion Brachial Plexus. Right Arm.* A. C., white, male, aged thirty-seven years, O-10911, admitted to the service of Dr. J. Chalmers DaCosta, Jefferson Hospital, April 26, 1926.

Chief Complaint.—Inability to use the right arm.

Present Illness.—January 10, four months ago, while walking along a bank, he stepped off a wall, falling a distance of about fifteen feet striking his right shoulder and head. He was unconscious for about an hour. On regaining consciousness in the house of a friend, the right arm was paralyzed. Six weeks later when the bandages were removed from the arm, there was no improvement.

Physical Examination.—Chest.—Negative with the exception of prominence of the right scapula and wasting of the muscle in this region. The right shoulder is lower than the left. Extremities.—Reflexes normal in the left arm and both legs. No œdema or tremors. Right arm hangs uselessly at his side when removed from the sling. There is total paralysis of the shoulder girdle muscles and complete sensory loss of the entire right arm and hand.

FIG. 2.—Case IV. Showing the return of power in case of complete right brachial paralysis. Operated upon four months after injury.

X-ray Report.—There is decalcification of the right acromion process in the region of the glenoid and of the right humerus in the region of the surgical neck and the greater tuberosity. There is no evidence of fracture or dislocation to account for this change; it does not seem to be the result of infection because there is no appreciable swelling in the soft parts. The left shoulder is apparently normal. There is no X-ray evidence of injury of any of the lower nine dorsal or upper two lumbar vertebræ. There is a synotosis between the sixth and seventh ribs in the paravertebral line.

Neurological Examination.—R. D. is present in all of the muscles of the right shoulder, arm and hand.

Operation May 8, 1926.—Incision exposed the brachial plexus, the sheath of which was opened; the plexus was obscured by a mass of scar tissue due to organized blood. It was almost impossible to isolate any definite nerve trunk because of the scar tissue. The fifth and sixth cervical trunks were finally identified and freed from scar tissue. Neurotomy was done on each of these nerves down to their subdivision. An end of a divided trunk, which they took to be the inner cord (the seventh cervical nerve) was freed from scar tissue. They were unable to find the proximal end of this trunk, so they implanted the distal end in the posterior trunk, after making numerous slits in the posterior trunk by means of a small cataract knife; "O" catgut was used to suture the distal end of the seventh nerve into the posterior trunk. Because of their inability to positively identify the structures and the uncertainty of where the implant was placed, an unfavorable prognosis was given to the family.

May 29, 1926.—Discharged. On day of discharge, three weeks after the operation, the patient had some movement in his right hand and some return of sensation. He complained of shooting pains down the arm and hand.

October 15, 1928.—Two years later. Patient re-admitted to Hospital with subacute appendicitis and post-operative brachial palsy.

Examination of Arm.—Left side normal. Right upper extremity: patient cannot abduct the arm or bring it posteriorly. He is able to draw the forearm forward weakly over the right chest. He cannot rotate it at the shoulder. Flexion power is absent. Also extension of forearm absent. He can pronate and supinate the hand. He has good flexion of the hand but extensor power is absent. Flexion of thumb and index finger normal. Remaining three fingers have moderate flexor power but can be only half extended. Hand grip fairly strong. Lifting power of hand and arm strong. Crepitation of right shoulder joint present on movement of shoulder. The patient can distinguish between sharp and dull over the entire extremity except in an area over the radial side of the forearm, extending from the elbow to the base of the thumb. In this area he has a constant "cold numb" sensation. Heat and cold tests normal excepting radial surface of forearm, bases of thumb and index finger—here the sensation is confused.

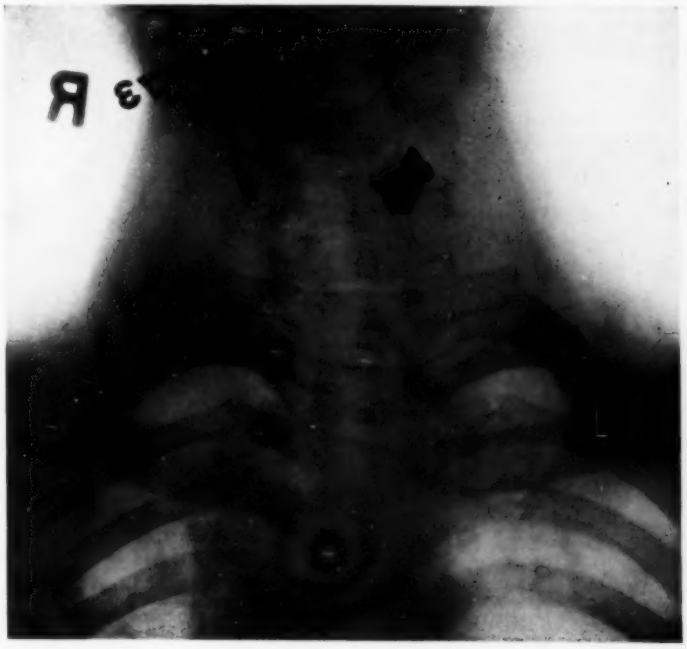

FIG. 3.—Case V. Shows bullet in the sixth cervical vertebra causing paralysis of the left arm.

October 17, 1928.—Electrical reaction. R. D. is present in the biceps muscle. In all other muscles of arm R. D. is not present.

Comment.—This patient was again seen in October, 1929, three and one-half years after the operation. See Fig. 2, Case IV. Sensation is practically normal throughout the right upper extremity. All functions of the arm and hand have returned except flexion of forearm. There is still weakness of the extensors of the wrist, but wrist drop is not present.

This illustrates the long interval between the injury and operation (four months). Some early return of muscle power, three weeks after operation, in muscles in which the electrical reactions of degeneration were present at time of the operation. It further emphasizes the protracted period (two years) before any marked improvement in muscle power was evident, and lastly, the amazing strength of the muscles and the complete return of sensation which occurred in the third year after operation.

CASE V.—*Left Traumatic Brachial Palsy, Due to Bullet Imbedded in Sixth Cervical Vertebra.* P. A., white, male, aged twenty-two years, R-9749, admitted to Jefferson

Hospital March 11, 1929. *Chief Complaint.*—Inability to use left arm. Sensory changes in dorsum of left hand.

Present Illness.—On the night of February 2, 1929, a .38 calibre bullet was inadvertently lodged in neck. He immediately lost the use of the left arm and left leg. Power in the leg began to return two days later. The use of the arm, however, did not return; on the contrary, the slight flexion use he had, at the elbow, was lost. He attributes this to an attempt of removal of the bullet at another hospital. This, of course, was not the case as only a superficial attempt was made to remove the bullet.

Physical Examination, March 11, 1929.—Five weeks after the injury. There is no loss of power or sensory loss in either leg. The reflexes are normal. There is a flaccid paralysis of the left arm, from and including the shoulder to the wrist. He can just move his fingers toward flexion; adducting and abducting function is lost. There is no complete sensory loss in the arm or hand except on the dorsum of the hand.

X-ray Findings.—There is an irregular triangular body, metallic, which is probably a .22 calibre bullet and which was mushroomed. It overlies the spinous process of the sixth cervical vertebra. It is laterally on the left side. There has apparently been some injury to the body of the vertebræ at the point of intact on the posterior aspect of the body.

Fluoroscopic examination on March 15, 1929, confirmed the above report.

Operation March 23, 1929.—An incision exposing the brachial plexus was made. There was no external evidence of trauma to the plexus. The sheath was not opened. The spinal column was reached across the posterior triangle of the neck. Dr. John Farrell localized the bullet lodged in the body of the sixth cervical vertebra and making lateral pressure on the spinal cord, the bullet was removed under the fluoroscope.

Progress.—The patient made an uneventful operative recovery. Sensation rapidly returned to the hand and the tingling, burning feelings abated. In two weeks he could flex, extend and abduct the fingers. In one month he could flex and extend the elbow. In six months he was able to write.

Comment.—This case represents trauma to the roots within the spinal cord. Fortunately, the roots were not divided. This case further shows definite spinal cord trauma, manifested by paralysis of the left leg for three days after the traumatism. During the seven weeks elapsing between the time of the injury and the operation, muscle power was being lost and not regained. It will be recalled that immediately after the injury he could flex his arm at the elbow, but three days later, he could not.

CASE VI.—*Gun-shot Wound of Axillary Plexus.* G. M., white, male, aged twenty-eight years, R-5285, admitted to Jefferson Hospital October 25, 1928. *Chief Complaint.*—Paralysis of left arm, burning sensation in fingers of left hand. Pain in left arm from elbow to hand.

Physical Examination.—Head.—Eyes.—Left pupil smaller than right pupil. Both react to light and accommodation. Ciliary reflex present. L. int. Rectus muscles possibly a little weak. *Surface of Chest.*—A puncture wound in the first interspace just lateral to the M. C. L. A second gun-shot wound on the summit of the shoulder, midway between the base of the neck and the tip of the shoulder. *Extremities.*—The left arm hangs limply to the side. He is able to weakly rotate the shoulder anteriorly and posteriorly. All other movements of arm, forearm and hand are lost, except abduction and adduction of the thumb (very weak). Some flexion power of the first and second phalanges of all of the fingers.

Sensation.—There is a gradual diminution of tactile sensation from the elbow to the hand; on the floor surface of the mid-radial region there is a small area of anæsthesia; on the floor surface of the thumb and index finger, tactile sensation is lost.

October 29, 1928.—Examination by Dr. Wm. Schmidt. Examination of arm shows complete R. D. in all of the muscles of the arm except the flexor muscles of the hand.

Operation October 30, 1928.—Incision exposing the axillary plexus by dissecting the pectoralis major muscle. A through and through gun-shot wound divided the

musculospiral; the median, musculocutaneous and circumflex nerves were traumatized but not divided and imbedded in scar tissue. The artery was not damaged. The scar tissue dissected from the nerves, neurotomy was done through the scarred area, the musculospiral nerve was anastomosed. The incision closed, a small rubber tissue drain introduced in the superficial parts.

December 20, 1928.—Discharged.

Comment.—Within one week following the operation the pain in the arm and hand had to be controlled by morphine; aside from this symptom, the progress in this case was slow. There was a gradual increase in the muscle power of the flexor group, so, that on discharge from the hospital, sensation, ten weeks after operation, was decidedly improved and he had a fair grip. During the subsequent six months, there was a gradual return of function of all of the muscles of the arm except the extensor group. The patient carried his hand in a Jones cock-up splint during this period, and he was given massage. He was not given electricity as it was unavailable in his home town. One year after the operation, he was again seen. He has extensor power returned. He drives his car and carries on his routine work.

CASE VII.—*Fracture of Cervical Vertebræ, Brachial Neuritis.* J. D., white, male,

FIG. 4.—Case V. Shows use of fingers after removal of the bullet from the body of the sixth cervical vertebra.

aged fifty-six years, O–5672, admitted to Jefferson Hospital November 1, 1925. (Professor DaCosta's service.) *Chief Complaint.*—"Stiff neck," pain and weakness in left arm.

Present Illness.—On October 27, 1925, patient, while at work, accidentally slipped and fell down about eighteen steps (wooden) hitting his head many times on the way down. The following day his neck was stiff, swollen, and painful, especially when he attempted to move his head. He noticed at times his inability to use arm but he attributed this to the excruciating pain in the arm which had been diagnosed as neuritis, because of sudden, sharp pain at onset, which has been more or less continuous since the accident.

Physical Examination.—Eyes.—Pupils irregular. Right pupil larger than left. Right pupil appears the more normal. No evidence of muscle inbalance. No conjunctivitis. Sclerotics a little injected.

Neck.—Rigid. Patient turns head on axis of body. No extreme rigidity of muscles of neck. Tenderness upon pressure over sixth to seventh cervical vertebræ. No palpable thyroid enlargement. No abnormal pulsation.

Chest.—Prominence of right side. Expansion fairly equal. Resonance throughout

except somewhat impaired at right apex posterior. Bronchial breathing right apex posterior. Tactile fremitus and vocal resonance increased on right side posterior except at base. Breath sounds generally clear elsewhere throughout. Occasional friction fremitus at left lower axilla.

Extremities.—Left arm and shoulder-joint. There is a point of tenderness about the size of a dime above the clavicle in middle which, upon pressure, causes referred pain down the outer side of shoulder, arm and forearm to finger tips. Upon direct pressure outer side of arm and forearm is "numb" to sensation; also palmar and dorsal aspect of fingers and thumb. Tenderness over mid-portion of spine of scapulæ. Pain referred down left arm when moving shoulder and elbow-joint. Left forearm thinner than right. No palpable axillary epitrochlear or supraclavicular glands. Radial pulse of good volume, regular in rate and rhythm and compressible.

X-ray Report, November 10, 1925.—There is a fracture of the posterior arch of the second cervical vertebræ with slight anterior subluxation of the second cervical vertebræ. There is evidently no lateral displacement. There is no evidence of tuberculosis in the chest nor any other pulmonary lesion.

Examination by Doctor Strecker, November 17, 1925.—The left upper forearm and hand show weakness and there is a considerable degree of atrophy which is especially noticeable in the forearm. The left arm is smaller than the right in all its dimensions, it is somewhat hard to believe that all the atrophy could have occurred in three weeks. The patient gives a history of fracture of shoulder five years ago and some of the atrophy may be due to this. The pain he describes is probably root pain and there is hyperæsthesia of the left upper extremity to pain stimulation. Probably there is some cord pressure.

December 5, 1925.—Discharged.

Comment.—This case was included in this series to emphasize the importance of ciliospinal reflex in cervical cord lesions. Had this been observed an earlier diagnosis would have been made. This case also emphasizes the rapid wasting of muscle. Observe Doctor Strecker's report! It is difficult to believe that all of the atrophy could have occurred in three weeks. Furthermore, had this case been diagnosed early and treated by the conservative plan, the rapid improvement which took place would have been credited to the conservative plan of treatment. The cause of the symptoms and signs was cord pressure, not brachial avulsion or traumatism. We are led to believe that some of the rapid cures by the conservative plan of brachial traumatism (not birth), belong in this group of cases.

THE CAUSE AND ELIMINATION OF REACTIONS AFTER INTRAVENOUS INFUSIONS*

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The history and application of intravenous therapy and medication especially as to the use of saline, glucose and acacia solutions has been completely and well reviewed in a recent article by Norman Keith of the Mayo Clinic. The value of infusions has generally become well accepted, but their effectiveness is often marred by untoward reactions, often at most inopportune times. It is the purpose of this paper to clear up the causes of these reactions and demonstrate practical methods to eliminate them. Reactions, as we know them, embody a variable extent of damage to the body physiology from mere elevation of temperature to chills, cyanosis, diarrhæa, nausea, vomiting, collapse and death. Even the mildest are uncomfortable to the patient and severe reactions are always dangerous, especially so in very ill cases, which are often, incidentally, the very cases wherein intravenous therapy can be of greatest value.

Many things have been suggested as causes for reactions, and to comprehensively study the problem each of the suggested factors was considered and either proven or disproven to be active factors in the situation. Thus rubber tubing, heat of solution, speed of injection, individual susceptibility, disease itself, hydrogen ion concentration of solution, absorption from glassware—all these have been suggested as possible causes. Of these, the first and seemingly most likely factor to be studied was the effect of hydrogen ion concentration. A portable quinhydrone unit was designed as illustrated (Fig. 1) using a Micslowitzer quinhydrone cup against standard saturated calomel electrode, and a Leeds and Northrup potentiometer. The temperature coefficient was placed on a graph in the top of the box so that readings made after equilibrium of the solution could be directly transposed to p^H and corrected for changes in temperature. This method gave readings of comparatively great accuracy within a few minutes' time. The accuracy of the method was challenged, however, because the solutions studied were unbuffered. It was therefore carefully checked with a colorimetric method, using brom-thymol blue. Fig. 2 illustrates in graphical form the result of this check. It is to be noted that there is an average variation of some 0.25 p^H between the two methods. This is, however, constant, and "salt action" of the indicator used in itself introduces a possibility of error, so that the true p^H probably lies somewhere between the two. We feel that the quinhydrone method is much the more accurate for relative differences of p^H and the observations made are therefore recorded in quinhydrone figures.

* Read before the Philadelphia Academy of Surgery, April 7, 1930.

The actual results as determined by carefully checked readings in some fifty-five infusions suggest strongly, with but one exception, that salines of

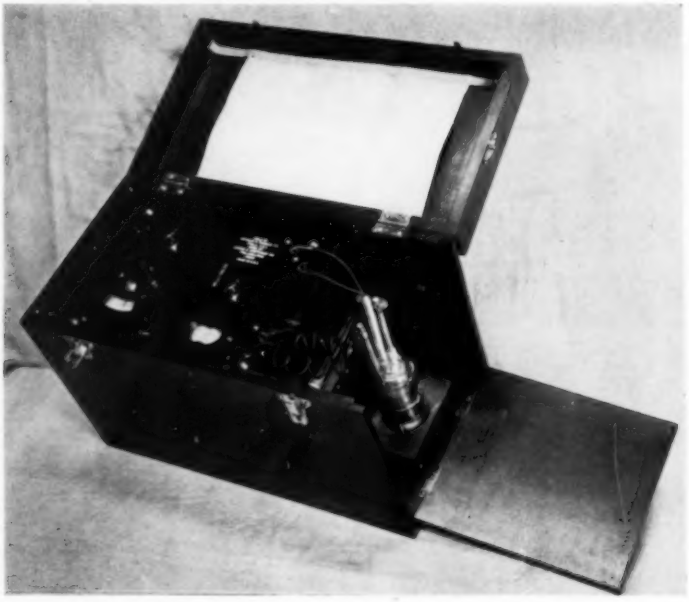

FIG. 1.—A portable Quinhydrone p^H determinator.

alkaline p^H are more prone to give reactions. It is to be noted (Fig. 3) that the line of division lies at a p^H of 7.05. By this means we were able to classify solutions used as pyrogenic, or reaction-giving and non-pyrogenic, being careful not to use solutions near the border line of p^H. Later only

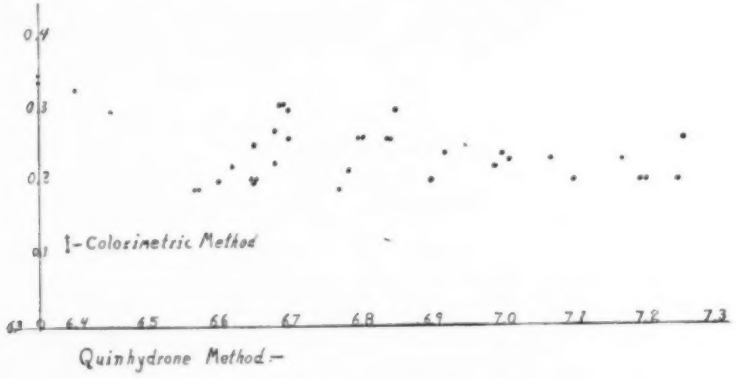

FIG. 2.—Check of Quinhydrone method.

water proven physiologically was so classified. That p^H in itself is not a causal factor was proven by buffering a solution of high p^H or pyrogenic, to a lower p^H, only to still have reaction occurring. Addition of ammonia to solutions of low p^H or non-pyrogenic caused no reactions, although the final p^H was over 8. The p^H of absolutely pure water, calculated from its dissociation constant,

should be 7.0, and the fact that solutions when freshly boiled, having pH higher than this cause reaction suggested strongly that alkaline impurities might be the causal factor, and this suggestion in turn led to chemical analyses of distilled water, which will be discussed later.

Individual susceptibility has been much discussed as cause, and this was next considered. A series of patients were given several infusions on sepa-

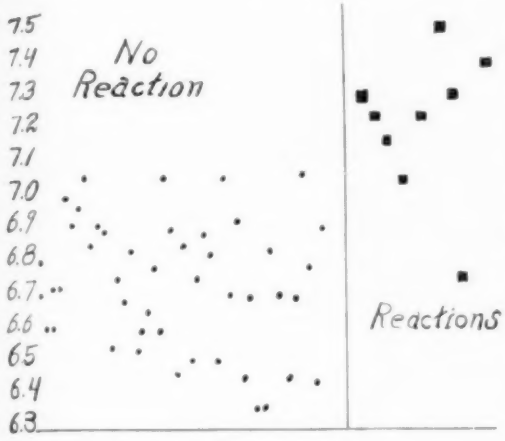

FIG. 3.—Reactions and pH.

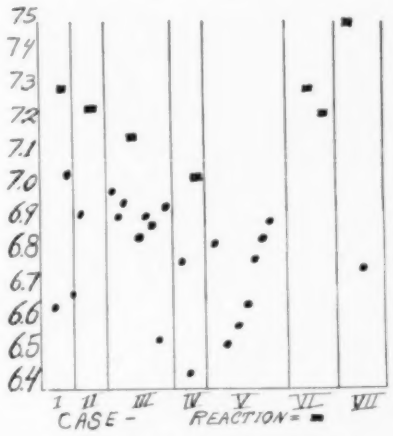

FIG. 4.—Individual susceptibility.

rate days or twice a day. Graphically illustrated Fig. 4 shows that each patient can react differently to various infusions, and not constantly in the same manner. It is also to be noted that the same pH indicator is still present in this series. Later work by injection of the true causal factor does show a slight variation of individual susceptibility to the chill-producing agent, but certainly not enough to explain the reaction itself.

TABLE I

Effect of Disease

Disease	Reaction	No Reaction	Percentage
Acute gall-bladder	4	11	36.3
Peptic ulcer	5	5	50.0
Sigmoiditis	1	7	14.0
Acute infection	1	1	50.0
Peritonitis	1	6	16.0
Miscellaneous	1	13	7.0
Totals	13	43	30.2 (Ave.)

Types and severity of disease were next suggested. Table I shows the inconstant percentages of reactions in five diseases, and one cannot help but conclude that disease is not a specific factor, since reactions occurred in all types. There is, however, a suggestion that severity of disease may increase susceptibility.

Rubber tubing was next ruled out by giving non-pyrogenic solutions through fresh rubber tubing, by boiling solutions with fresh rubber corks so that the final solution smelled strongly of rubber, all of which produced no reaction. Many of the above infusions, both with and without reactions, were, moreover, given through the same tubing.

The chill-producing effect of glucose and sodium chloride per se were next ruled out. Glucose of many lots and of various manufacturers were used, either prepared in distilled water, or given with saline, or in concentrated form, from ampoules. The latter never gave reactions, and the absence or presence of reactions in the former methods was entirely inconstant. Many reactions have also been observed following infusions of saline without glucose. Once more an accusing finger seems directed to distilled water, which was absent in concentrated ampoules. Both buffered and unbuffered solutions were used, but no differential result could be noted.

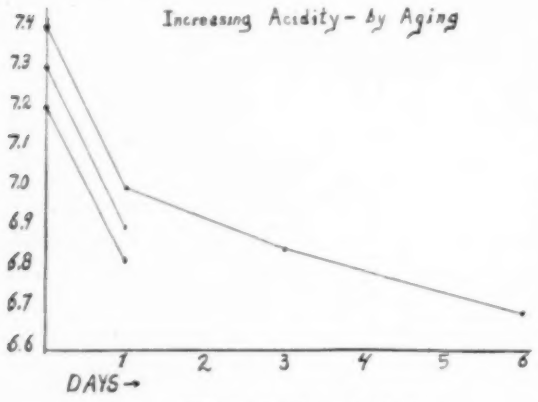

FIG. 5.—Effect of aging of solutions.

Temperature of solution has been much emphasized and many appliances are on the market now to keep up the temperature of infusion solutions. Non-pyrogenic solutions were given at 20° C. and at 110° F. without producing reactions. When too hot the patient complains of burning at the site of injection, but no reaction occurs. On the other hand, administration of cool fluids to patients with high temperature often has seemingly caused a drop of body temperature without reaction or chill. It is to be noted also that all the infusions above tabulated were given as near body temperature as possible, yet reactions occurred. The work of Swale Vincent may be cited here, but the reactions observed by him were those affecting blood-pressure, and no mention was made of other reaction.

Speed of injection is another possible cause emphasized by many who say that slow injection will prevent reactions from occurring. Non-pyrogenic solutions given at the rate of 1000 cubic centimetres in ten minutes through a large-bore needle gave no reaction. Pyrogenic solutions given at a rate of 1000 cubic centimetres per hour produced their usual reactions.

With the ruling out of all these extraneous factors and the constantly appearing suggestion of alkaline impurities as a causal factor, attention was next centered upon the nature and amount of that possible impurity and a careful study was made of distilled water. The p^H of distilled water was found to vary from 5.9 to 7.3 in examination of twenty-five bottles. Making up into saline did not change the original p^H, but fifteen minutes' boiling in

the autoclave caused a rise of p^H from 0.2 to 1.0 in various samples. This p^H after boiling rapidly fell at a definite rate, as illustrated in Fig. 5. This fall has no effect on reactions, since the solution of high original p^H still gave reaction at the low level illustrated. Reboiling will bring the p^H back to the original. Sterilization excludes the action of bacteria or their products as cause of this drop on aging. Its rapid occurrence and ready reversibility lead one to believe that this is purely a chemical absorption of gases, probably carbon dioxide from the air. The p^H in boiled solutions causing reactions suggests, however, the presence of an alkaline, non-volatile substance as causal factor, and analysis of distilled water was undertaken.

Two samples were used, pyrogenic (p^H 7.5) and non-pyrogenic (p^H 6.7) whose properties were proven physiologically to be such. Table II shows the differential analysis. Total solids were analyzed by evaporation at low temperature in platinum dishes until dryness. The inorganic fraction was determined by flaming to white heat, and the organic calculated by the dif-

TABLE II

Differential analysis

	Pyrogenic	Non-pyrogenic
p^H	7.5	6.7
Total solids	3.4 mgm/L	3.2 mgm/L
Organic solids	2.2 mgm/L	1.2 mgm/L
Ammonia	0.69 mgm/L	0.34 mgm/L
Inorganic solids	1.2 mgm/L	2.0 mgm/L
Ammonia content (distilled)		
First fraction	0.532 mgm/L	0.157 mgm/L
Residue	0.159 mgm/L	0.181 mgm/L
Bacterial count	150,000 per L.	550,000 per L.

ference. Organic content was again checked by a rather rough titration with permanganate and its reduction on heating. Ammonia was determined by a modified Nessler method. The greater amount of combined ammonia and organic matter in the pyrogenic water is to be noted especially. The first fragment of pyrogenic water distilled at 105° C. shows a considerable amount of ammonia. At this temperature precipitation occurs of a brownish, gelatinous material, and ammonia is driven over, showing the unknown compound to be split at 105° C.

Because of this, some pyrogenic water was distilled under vacuum at 35° C. No water trap was in the system and the first fraction when injected into a dog produced severe reaction. The middle fraction was non-pyrogenic, but the residue gave severe sustained fever without great chill. This is illustrated in Table III. Bacteria then attracted our attention and plating revealed the huge numbers of bacteria shown in Table II. The greater number was, however, present in the non-pyrogenic water and it was our intention to study the various types of bacteria and their products when the papers of Dr. Florence Seibert and her colleagues were discovered. All the results so

TABLE III

Reactions in dogs

Substance	First fraction	Second fraction	Residue
Pyrogenic water	++ 18 cc.	−− 150 cc.	++ 19 cc.
Non-pyrogenic water	−− 5 cc.		−− 5 cc.
Non-pyrogenic N.S.S.	−−		
Non-pyrogenic N.S.S. and ammonia	−−		

far described corroborate in every detail the work reported by Doctor Seibert during her years of study of this problem. Thus even fractional distillation revealed the same results, except that she was able to eradicate the pyrogenic property of the first fraction by use of a water trap, as illustrated in Table IV.

Her work continued farther, however, in that she isolated the bacteria as belonging to a group of river bacteria classified in Jordan's classification as Groups X and XI. She definitely and conclusively proved that reactions were caused by the toxic products of these bacteria and not the bacteria

TABLE IV

Dr. Florence Seibert

Original water	First fraction	Second fraction	Residue
++	++	−−	++
+	+	−−	++
	Water trap interposed		
++	−−	−−	++
++	−−	−−	−−
++++	−−	−−	++++

themselves and showed how easily water could be contaminated by them. These experiments have been repeated by us with essentially the same results.

It is of interest to note that the quantity of pyrogenic water necessary to produce reaction may be very small, since ten to one hundred cubic centimetres may easily give a severe reaction as demonstrated by Doctor Seibert and corroborated by us in a series of cases. Pyrogenic substances can occur in forty-eight hours after contamination, unless the water be first sterilized to prevent growth of organisms. Moreover, only the most efficient of spray traps will prevent the first fraction causing reactions, as we have shown in a recent series of infusions.

Practical application of these combined results is simple and easy. Single distillation by a suitable apparatus, preferably a still containing a multiple Baffle Plate spray catcher, or Glinsky tube, with immediate sterilization and absolute seal will make solutions permanently reaction-free, unless the seal is broken. The essential feature to be stressed again and again is the necessity of water-trap distillation, to prevent mechanical carrying over of toxins, and immediate sterilization and seal to prevent growth of bacteria. Triple dis-

tillation is not essential if the above precautions are carried out, but they must be carried out accurately and carefully since the tap water used for distillation contains much of the pyrogenic substances and any flaw in the above mechanism, either in inadequate apparatus, or delay in sterilization, will nullify all other efforts or precautions taken to prevent reactions. It is the hope of the author that by bringing these facts more definitely before our clinicians that reactions following intravenous infusions may become a thing of the past.

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HYPERPARATHYROIDISM

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Since the discovery of the parathyroid glands by Sandström, in 1880, an occasional case of parathyroid hypertrophy or tumor has been reported in patients with osteomalacia, osteitis fibrosa, paralysis agitans, rickets, tetany, chronic nephritis, and epilepsy. DaCosta, in 1909, could find only seven cases reported in the literature. He added one more. In five of these the condition was found incidentally at necropsy; three were operative cases but did not present pathognomonic features. Hoffheinz, in 1925, reviewed pathologic reports of forty-five cases of enlarged parathyroid glands. In twenty-seven of these, there was disease of the skeleton (osteitis fibrosa, seventeen; osteomalacia, eight; and rickets, two). Lloyd, in a recent review of 10,000 consecutive necropsies, found five parathyroid tumors. As early as 1903, Erdheim commented on the frequency of the occurrence of the combination of the foregoing diseases of bone and parathyroid tumors. He advanced the hypothesis that the parathyroid enlargement might be an inadequate attempt at compensatory organic hypertrophy effected by the pathologically disturbed calcium metabolism. On the basis of this, Mandl, in 1925, transplanted healthy parathyroid glands into a patient with generalized osteitis fibrosa, but this had no effect on the progressive course of the disease. He then explored the region of the parathyroid glands and removed a parathyroid adenoma. Following this, the patient spectacularly improved. This led Mandl to conclude that in some cases, at least, the parathyroid tumor is primary and the bony changes are secondary. Nine cases have been reported with some or all of the features of the syndrome which Barr, Bulger, and Dixon called hyperparathyroidism. In five of the nine cases, operation was performed and tumors were removed. In one case of the nine, two apparently normal, but undoubtedly hyperfunctioning, parathyroid glands were removed. Three patients were not operated on and there is no proof of the presence of tumors, but many of the clinical features were present.

The clinical features to be noted in general are (1) high concentration of serum calcium; (2) low concentration of serum phosphorus; (3) abnormal excretion of calcium in the urine; (4) rarefaction of bones; (5) occurrence of multiple cysts or tumors of bones; and (6) hypotonia and muscular weakness. A negative calcium balance might properly be included, since in every case in which studies of excretion of calcium and phosphorus were done, a negative calcium balance was found, except in the case of Wilder's patient. In this instance the determinations were done several days after the institu-

tion of a high-vitamine diet and daily exposures to ultraviolet light. This the author considered to be the cause of the slightly positive calcium balance found at that time. Following the removal of the parathyroid tumor these studies were repeated and huge amounts of calcium were found to be retained.

In the five cases of parathyroid tumor and the one case of hyperfunctioning parathyroid glands, the sexes were equally divided and the ages ranged from twenty-eight to fifty-six years, as far as is known. The age of the patient in the case reported by DuBois, Aub, Bauer, and Richardson's patient is not known. All the patients were weak, tired, and were either unable to walk or found difficulty in walking. All but one had pain. The pain was prone to affect the extremities. If the patients could assume the upright position, the posture was poor. Kyphosis, dorsum rotundum, and bow legs were to be seen in various cases. Polydipsia and polyuria seemed to have some significance, although they were not constant symptoms. At some time during the course of the disease, frequently early, attacks of nausea, vomiting, and abdominal pain, associated at times with marked constipation, were to be noted. This was especially evident in the cases reported by Gold and by Boyd, Milgram, and Stearns. These attacks disappeared promptly on removal of the parathyroid tumor. Muscular weakness, hypotonia, and lassitude were noted in a number of cases, especially in the cases reported by Mandl, by DuBois, Aub, Bauer and Richardson, and by Barr, Bulger and Dixon. Rarefaction of bones was present in every proved case and in all but one of the unproved cases. This was always so marked as to be called osteitis fibrosa cystica on the basis of the röntgenograms. Fractures of these rarefied bones were reported in half of the cases. Multiple cysts or tumors of the bone were frequently encountered. Loss of weight was usually marked, and, in some cases, extreme.

In each of the five cases in which a parathyroid tumor was removed and in the one case in which hyperfunctioning parathyroid glands were removed, there was striking improvement in the clinical picture after the first few days. Usually, immediately after the tumor is removed, these patients show evidence of tetany. Immediately after operation the high concentration of serum calcium dropped to far below normal, and it was usually weeks before it gradually rose to within normal limits. In those cases in which metabolic studies of calcium and phosphorus were done after removal of the parathyroid tumors there was marked retention of both. In the case reported by Boyd, Milgram, and Stearns, there was a remarkably rapid and complete return to normal of the urinary symptoms and signs soon after the operation. The tumors removed in four of the cases were adenomas, and in one case the tumor was malignant. Wellbrock, in 1929, renewed the subject of malignant adenoma of the parathyroid glands.

Duken reported two of the three cases in which operation was not done. Both patients presented some of the features of hyperparathyroidism.

One patient died of generalized sarcomatosis some time after the original

report of the case was printed, and in the other case an operation was not done, so neither of these cases can be accepted as proved. Box and DeWesselow, in 1925, reported a case of "chronic nephritis with possible parathyroid syndrome." This case presented many of the features of hyperparathyroidism but the suspicion that a parathyroid tumor was present was not confirmed by operation or necropsy.

The case reported herewith is the seventh proved case of hyperparathyroidism and the sixth in which this condition was due to tumor. These cases record a remarkably complete and relatively new clinical syndrome. Based on knowledge of the physiology of the parathyroid glands, as recently demonstrated by Collip, by Greenwald and Gross, by Albright and Ellsworth, and by others, these cases represent exactly what one would expect if the body were subjected to an excess of the parathyroid secretion over a relatively long time. Albright and Ellsworth recently made complete studies on a young Italian boy whose condition they had diagnosed as hypoparathyroidism. The criteria on which this diagnosis was made were (1) low serum calcium; (2) high serum phosphorus; (3) cataract; (4) normal density of bones; and (5) aggravation of tetany by exertion. All of the cases referred to in this report demonstrate exactly converse changes.

Report of Case.—A girl, aged fourteen years, registered at The Mayo Clinic November 23, 1929. The chief complaint was of spells of vomiting, pallor, and loss of weight. She had always been healthy and robust until about sixteen months previously. In July, 1928, she had begun to be a little pale, to lose weight, and to be generally below normal physically. Her weight had decreased from eighty-six to fifty-five pounds from the onset of her trouble to the date of admission. Beginning in the summer of 1928 she had become constipated and had required cathartics until two months before her admission, when movements of her bowels had become, and had remained, fairly regular. October 4, 1928, she had had her first spell of vomiting. This had lasted twenty-four hours. During this period she had been unable to retain anything in her stomach. After that time, the spells had recurred at intervals of never more than two weeks and had lasted from one to five days. These attacks had seemed to appear without cause. Food did not act as a predisposing cause. Between attacks she could eat anything with impunity. The last attack had begun one week before her registration at the clinic and had continued five days. She had had polydipsia and polyuria, with consequent

Table I

Variations in blood serum calcium and phosphorus

Date, 1929	Calcium milligram in each 100 cubic centimetre	Phosphorus milligram in each 100 cubic centimetre
November 4	16.32	2.46
November 5	17.67	2.80
November 15	15.50	3.2
November 16	Operation	
November 18	7.89	2.2
November 25	7.74	3.41
November 29	7.56	3.9
December 5	7.85	4.04
December 12	10.36	3.57

nocturia three to five times each night for the preceding year. She consistently drank about two quarts of water each night.

The patient weighed fifty-five pounds, whereas the standard weight for her height and age was ninety pounds. She was pale, emaciated, and appeared to be chronically ill. Electrical irritability was decreased. Otherwise, the general examination gave essentially negative results.

Complete gastro-intestinal studies did not reveal organic lesions. The blood count revealed moderate secondary anæmia. Urine varied in amount from 750 to 3150 cubic centimetres; specific gravity, on daily examination varied from 1.004 to 1.010. The urine usually contained a trace or a faint trace of albumin and occasionally a few pus cells. Excretion of phenolsulphonephthalein on one occasion was 40 per cent. and on another 45 per cent. in two hours. The concentration of blood urea on the day of admission was 80 milligrams in each 100 cubic centimetres. The following day it was 37 milligrams in each 100 cubic centimetres and it never thereafter rose above 40 milligrams. In Table I are given the variations in the concentration of serum calcium and serum phosphorus during her stay at the clinic. Röntgenograms of all the bones gave evidence only of diffuse decalcification, without loss of normal structure of the bone (Figs. 1, 2 and 3). Repeated tests of water concentration were done, all of which disclosed definite fixation of specific gravity. Polydipsia or polyuria were not constant while the patient was under our observation. A study, for three days, of calcium and phosphorus in the urine and the stool revealed a slightly positive phosphorus balance and a slightly negative calcium balance.

FIG. 1.—Generalized rarefaction of femurs and tibias.

In view of the similarity of this case to several of the other cases of hyperparathyroidism, a tentative diagnosis of parathyroid tumor was made, although careful palpation of the neck with this in mind did not reveal tumor in the parathyroid region.

November 16, 1929, operation was performed. The thyroid gland was found to be about normal in size, but it contained a little more colloid material than normal. Lying behind the left lobe of the thyroid gland at the inferior pole and outside of the capsule but attached thereto, was a tumor which measured 1.5, 1.25 and 1.25 centimetres in various diameters (Fig. 4). It was definitely brownish and the contrast in color between the tumor and remainder of the thyroid gland was marked. The color and situation of

the tumor indicated it to be an adenoma of the left inferior parathyroid body. The tumor was removed. Other parathyroid bodies could not be seen. The right lobe of the thyroid gland was elevated also and there was no tumor behind this. Nothing was done

FIG. 2.—Generalized rarefaction of skull.

FIG. 3.—Generalized rarefaction of pelvis.

to the thyroid gland. Pathologic study of the tissue removed (Fig. 5) disclosed that it was a parathyroid tumor (adenoma) weighing 16 grains (1 milligram).

The effect of the operation was remarkable. The following day the patient complained of numbness and tingling in the fingers and toes, and Chvostek's sign was present

FIG. 4.—Gross specimen of parathyroid adenoma. Dimensions 1.5, 1.25 and 1.25 centimetres in various diameters.

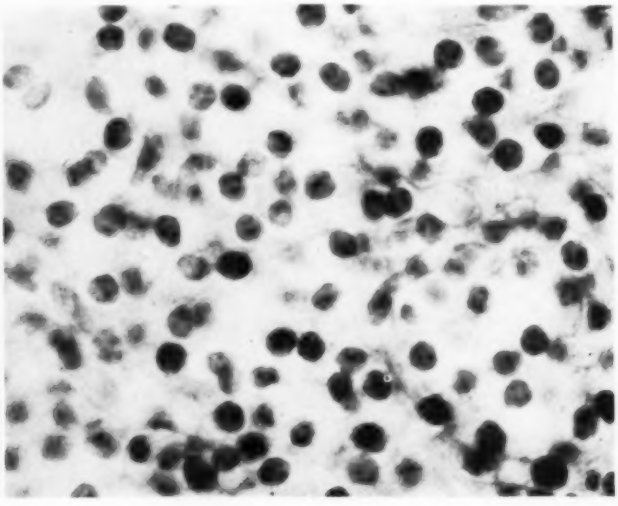

FIG. 5.—Structure of parathyroid adenoma (x 750).

at irregular intervals for several days. The tingling and numbness became worse, and November 19, 5 cubic centimetres of solution of calcium chloride, 10 per cent., administered intravenously, gave relief even before the injection was completed. Later the same day the sensation returned to a lesser degree and was relieved by 10 units of parathyroid extract-Collip (para-thor-mone) given subcutaneously. Beginning a few hours after the

operation, cod-liver oil, viosterol, and calcium chloride were administered daily. The second day after operation the concentration of serum calcium was 7.89 milligrams and

TABLE II

Studies of metabolism of calcium and phosphorus†*

	Three days pre-operative, average, gram		Three days post-operative, average, gram	
	Calcium	Phosphorus	Calcium	Phosphorus
Intake	5.36	4.62	4.485	3.85
Output				
Urine	1.474	2.38	0.03	0.725
Stool	4.10	1.36	2.03	0.740
Total	5.57	3.74	2.06	1.46
Balance	—0.21	+0.88	+2.42	+2.39

* Determinations of inorganic calcium were done according to the method of Kramer and Tisdall except that acidity was adjusted to pH 4.8 to 5.2, the indeterminate range of methyl red; this is according to Shohl.

† Determinations of phosphorus were done according to the method of Fiske and Subbarow.

of phosphorus 2.2 milligrams in each 100 cubic centimetres. It was not until December 12 that the concentration of serum calcium and phosphorus returned to normal limits (Table I). Studies of metabolism a few days after operation revealed a markedly positive calcium balance (Table II). Electrical excitability of the nerves approached normal (Table III). After operation the amount of urine remained practically the same as before operation. Excretion of phenolsulphonephthalein was again 45 per cent.

TABLE III

Contraction caused by electrical stimulation of ulnar nerve

Milliamperes

Date, 1929	Kathodal closing	Anodal closing	Anodal opening	Kathodol opening	Kathodol closing tetanus
November 13	1.8	2.8	4.8	5.2	5.8
December 11	1.2	2.2	3.8	5.6	6.4

The water concentration tests before operation revealed a striking loss of ability to concentrate fluids (Table IV). In none of the tests done before operation did the specific gravity rise above 1.015 and in none of the tests done within four weeks after the operation did the specific gravity reach 1.017. Polydipsia and polyuria were less marked after operation, although this had seemed to occur with some irregularity previously. It was

TABLE IV

Water concentration tests

Date, 1929	Time	Amount, cubic centimetre	Specific gravity
November 1	11 a.m.	95	1.011
	2 p.m.	70	1.014
	5 p.m.	70	1.015
	8 p.m.	75	1.013
	8 a.m.	300	1.011
November 4	11 a.m.	225	1.009
	2 p.m.	200	1.010
	5 p.m.	175	1.010
	8 a.m.	200	1.010

Date, 1929	Time	Amount cubic centimetre	Specific gravity
November 9	11 a.m.	150	1.010
	2 p.m.	100	1.011
	5 p.m.	50	1.010
	8 p.m.	125	1.010
November 16	Operation		
December 6			
	5 p.m.	270	1.012
	8 p.m.	75	1.015
	8 a.m.	450	1.015
December 12	11 a.m.	75	1.016
	2 p.m.	140	1.014
	5 p.m.	175	1.015
	8 p.m.	100	1.015
	8 a.m.	450	1.013

never as marked while the patient was in the hospital as before admission. Appetite was noticeably improved and there were no more vomiting spells. Röntgenograms of the bones taken after operation did not give evidence of increase in density.

Comment.—Albright and Ellsworth, on the basis of their work and of that of Albright, Bauer, Ropes, and Aub, suggested the following hypothesis of the mode of action of parathyroid extract-Collip (para-thor-mone). This seems a most logical hypothesis to account for the changes in the reported cases of hyperparathyroidism. "When parathormone is administered, the equilibria of the body fluids are upset in such a way that an increased phosphorous excretion is a necessary result. We do not know the cause of the increased phosphorous excretion, but as a result of this increased phosphorous excretion the body fluids become depleted in phorphorus. The falling serum phosphorus is evidence of this. As the phosphorus and consequently the phosphate ions in the serum fall, there is a tendency to an unsaturation of the blood with calcium phosphate. This tendency is met by a mobilization of calcium from the bones. Thus a deficit of phosphate ions is being supplied by calcium and phosphate ions. Consequently the serum calcium rises. With a rise in serum calcium, provided the level is not below the threshold for calcium excretion, there is a rise in urinary calcium output."

When the patient in Albright and Ellsworth's case of hypoparathyroidism was under the influence of parathyroid extract-Collip (para-thor-mone) they noted marked polyuria at night. This fact and the presence of polyuria and more or less fixed specific gravity in many of the cases of hyperparathyroidism leads one to suspect disturbed water balance rather than true renal injury. This view is strengthened by the complete, and, at times, rather rapid, return to normal of renal function after removal of a parathyroid tumor.

The occurrence of osteitis fibrosa, multiple giant-cell tumors, and bone cysts, has been explained by Gescheckter and Copeland. They considered that a cyst of bone is an arrested giant-cell tumor; that its formation is a reparative process; and that if multiple cysts and giant-cell tumors are present, some

complicating factor is present which prevents the giant-cell tumors from forming cysts of bone. They presented cases of osteogenesis imperfecta, rickets, syphilis, fragilitas ossium, and osteomalacia in association with multiple cysts of bone and giant-cell tumors.

The general picture of osteitis fibrosa and, in many cases, the occurrence also of multiple cysts of bone and giant-cell tumors, is exactly what one would expect if one accepts Geschеckter and Copeland's theory as to their formation. The pain and weakness in the extremities are the direct results of the bony and muscular changes, which are themselves accounted for by the excess of parathyroid secretion in the blood-stream. This also explains the high concentration of serum calcium, the low concentration of serum phosphorus, and the negative calcium balance. There is excellent corroboration of this in the experimental work of Collip and others. Certainly the occurrence of hyperparathyroidism, with its train of changes in bone, would be an ideal complicating factor.

There is no adequate explanation for the frequent occurrence of gastro-intestinal symptoms in the group of cases which has been reported in the literature and which were present in the case reported in this paper. In five cases constipation was a prominent symptom, and in the same cases attacks of abdominal pain accompanied by vomiting had been the outstanding feature of the disease at some time during its course. Frequently these were early manifestations and had entirely disappeared before the patient was admitted to hospital.

The same also might be said of the urinary symptoms. In one case the presence of a renal pelvis full of stones, on which was superimposed a pyogenic infection, would satisfactorily explain the symptoms. In none of the other three cases in which these symptoms were marked was there a suitable or even a plausible explanation unless the hypothesis advanced by Albright and Ellsworth is to be accepted. Accepting the disturbance of water metabolism as the cause of the renal dysfunction, when so little is really known about this subject itself, is to open a question over which there has been considerable controversy. However, we can think of no other explanation which would so satisfactorily explain the rapid return to normal of some of the urinary symptoms after the parathyroid tumor was removed.

Our patient is the youngest who has been proved to exemplify the clinical syndrome which is the subject of this paper. The symptoms of this patient were of shorter duration and the chief complaints related to the gastro-intestinal and genito-urinary systems rather than to the osseous system as in all the other cases. Although the röntgenograms of bones did reveal evidence of diffuse decalcification of all the bones, they certainly did not disclose anything that was characteristic for osteitis fibrosa. We have no means of knowing to what extent the process in the bones would have gone had the parathyroid tumor not been removed. Probably the patient would have had symptoms referable to the osseous system had the negative calcium balance persisted for a sufficiently long time. Following operation the gastro-intes-

tinal symptoms promptly cleared up as has been the case in the other cases reported. The return of renal function to normal has not been so rapid as in some of the other cases. Six days after operation the excretion of phenolsulphonephthalein was the same as before. The water concentration tests revealed slight improvement in the ability of the kidneys to concentrate fluids. Electrical reaction was not markedly lacking before operation, but it was practically normal a few days after operation. Röntgenograms of bones four weeks after operation did not reveal increase in density.

SUMMARY

A case of hyperparathyroidism in a young girl is described in which symptoms were due to excessive parathyroid secretion caused by a parathyroid adenoma. The symptoms and data include progressive weakness and loss of muscular tonus, attacks of abdominal pain and vomiting, anæmia, polydipsia and polyuria, hypercalcemia and hypophosphatemia, and diffuse decalcification of the skeleton. Data concerning six other proved cases and three not proved by operation were gathered from the literature.

The surgical removal of the parathyroid tumor in the case reported was followed by marked relief from all symptoms.

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THE TREATMENT OF ACUTE EMPYEMA THORACIS

WITH A REPORT OF 153 CONSECUTIVE CASES

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This paper does not attempt a comprehensive survey of the methods of treating empyema. We wish only to note briefly the present physiological and pathological principles underlying its treatment, to present the method of treatment used at the New Haven Hospital and to report the results.

This disease has been recognized since the days of Hippocrates. The development of therapeusis has been slow, at times even stationary, until the latter part of our modern era of surgery. During the World War the work of the Empyema Commission with Graham, Bell and others did much to formulate the present concepts of physiology and pathology needed in the sane treatment of this disease. A tremendous operative mortality has been reduced to almost nothing while morbidity in the form of chronic empyema is rapidly decreasing.

It is now generally recognized that a diagnosis of empyema does not necessarily constitute an indication for immediate operation. It has been learned that the sudden change of a normal negative intrathoracic pressure to a pathological atmospheric pressure may result in respiratory failure; from collapse of the lung, mediastinal shift, and reduction in vital capacity where vital capacity is already lowered by disease. Attention has been drawn to the cardiac embarrassment from mediastinal shift and kinking of the venacava and other vessels. The postponement of an open thoracotomy until the pulmonary lesion subsides, the vital capacity becomes more normal, and adhesions between the parietal and visceral pleura stabilize the intrathoracic organs, means that no deaths will follow the acute operative pneumothorax from collapse of the undiseased lung.

On the other hand adequate drainage just as soon as it can be obtained safely is to be desired because the pleura rapidly thickens, adhesions quickly form and the cavity becomes more rigid, thus militating against re-expansion of the lung and obliteration of the empyema cavity. There is then the danger of pulmonary collapse from an operative procedure done too early and the danger of chronicity from an operative procedure done too late.

It is also generally recognized that this intrathoracic process varies with the type of infection. In a streptococcus pneumonia, the pleura is infected early and a well advanced pleurisy may be associated with a still prominent intrapulmonary infection. In a pneumococcus pneumonia the pleurisy is often a late manifestation and the pneumonic process may have run its course before the pleurisy becomes a serious affair.

Aspiration, intercostal drainage, rib resection, double intercostal drainage with irrigation, radical thoracotomy with closure and intercostal drainage below, intercostal drainage with tidal irrigation, or various combinations and modifications of these methods are in vogue in various parts of the country. An evaluation of each type of treatment is not the purpose of this paper. The value of intercostal drainage and the value of open thoracotomy with their dangers and their faults is generally known and understood. Whatever method is used, it should yield a low mortality, a complete healing and restoration of pulmonary function, the shortest possible convalescence and at the same time be as simple and practicable as possible.

The mortality with various types of modern treatment properly carried out is much the same. A fatality should never result from the empyema itself. Death does occur in a certain number of instances due to the intra-

MORTALITY

TABLE I

Relation to Organism

Organism	No. cases	Deaths	Per cent mortality
Pneumococcus Type I	36	2	5.5
Pneumococcus Type II	5	2	40.
Pneumococcus Type III	7	0	0
Pneumococcus Type IV	15	2	13.3
Pneumococcus Type undetermined	15	2	13.3
Streptococcus hemolyticus	25	3	12.
Non Hem. streptococcus	12	0	0
Staphylococcus aureus	9	2	22.2
Staphylococcus albus	0	0	0
Unknown or mixed	29	4	13.7
Total	153	17	11.1

pulmonary process, septicemia, multiple infections, pericarditis or other complications. Incomplete healing, however, varies with the different types of treatment, the care with which the treatment is carried out, etc., and reports of chronicity range from 0 to 50 per cent. Chronicity in non-tuberculous empyema is generally understood to result from one or more of the following causes: Improper drainage, an operative procedure done too early, one done too late, foreign bodies in the pleural cavity or osteomyelitis of the ribs. The most important of these is improper drainage. All of these causes should be preventable.

The period of convalescence likewise varies with the method used, but also depends upon the type of the infecting organism, the severity of the infection and the time in the disease when the treatment is instituted. That the method should be as simple as possible goes without saying, but important features in the treatment should not be omitted for the sake of simplicity.

The treatment for acute suppurative pleurisy used at the New Haven Hospital was worked out by Dr. Joseph Marshall Flint, formerly professor

of surgery at Yale, and is based on the physiological principles discussed. The better features of the closed method of treatment have been combined with those of the open method. Plugging of the drainage tube, the great criticism of the closed method, has been corrected by rib resection and the use of a large tube, while the value of negative intrathoracic pressure has been retained by a special type of tube and constant suction. We believe that suction is a very important feature in our treatment. A quantitatively controlled and continuous negative pressure aids re-expansion of the lung and obliteration of the cavity, but most important of all it keeps the pleural cavity empty of secretions. The so-called "operative shock" of opening the thorax has been largely reduced by careful local anæsthesia and avoidance of wide-open exploration. Rib resection has been delayed until the intrathoracic pathology has undergone enough change to make it safe, but repeated aspirations have checked the mechanical dangers and alleviated the absorptive features of the pleurisy. It is believed that this delay has not increased our

TABLE II
Relation to Age

Age group	No. cases	Deaths	Per cent mortality
Under two years	23	5	21.7
2–12	69	4	5.7
12–40	47	6	12.7
40–	14	2	14.2
Total	153	17	11.1

6 deaths last 83—7.2 per cent

mortality, and that it has not resulted in chronicity is shown in our results.

The outline of our treatment is as follows: A diagnosis is made as early as possible and is followed by a microscopic and cultural study of the infecting organism. Treatment by repeated aspirations is carried out, using precautions to prevent infections of the thoracic wall, until the pulmonary process is minimal, the thoracic organs more or less fixed and the specific gravity of the pleuritic fluid has increased to such an extent that it cannot be readily drawn through the aspirating needle. When the pleuritic fluid is frank pus, rib resection is usually safe, but this alone should not be the criterion for selecting the time of operation. As previously stated the pneumonic process must be evaluated and the character of the infecting organism must be known. A pneumococcus pleurisy may be operated upon long before the pleuritic fluid becomes so thick that it cannot be aspirated and the operation should be done just as soon as it is safe. Rib resection using novocaine anæsthesia is then carried out. The technic we use is as follows: The location of the incision, if possible, is at the midaxillary line at about the level of the eighth or ninth rib so that the tube externally is well above the bed and the intrathoracic portion of the tube is high enough to be away from a rising diaphragm. This location obviously must vary in many cases. All

rib resections are preceded by needling on the operating table and the pleura is opened only when the pleura has yielded fluid. A rib is then resected for a distance of four to eight centimetres, being careful that no rib is left uncovered by periosteum. In the two cases of osteomyelitis of the rib in this series this precaution was not carried out and the bared rib ends were covered with bone wax. If the rib ends are rongeured well into the periosteal covering, the danger of osteomyelitis is small. The pleura is then opened using a small incision in the base of the rib bed and air is allowed to flow into the thoracic cavity slowly so that any readjustment here will not be sudden. If no respiratory difficulty is encountered, the opening is enlarged and the fluid and fibrin clots are evacuated by aspiration. Fibrin clots may be floated up to the pleural opening with saline and removed, if the cavity is well walled off.

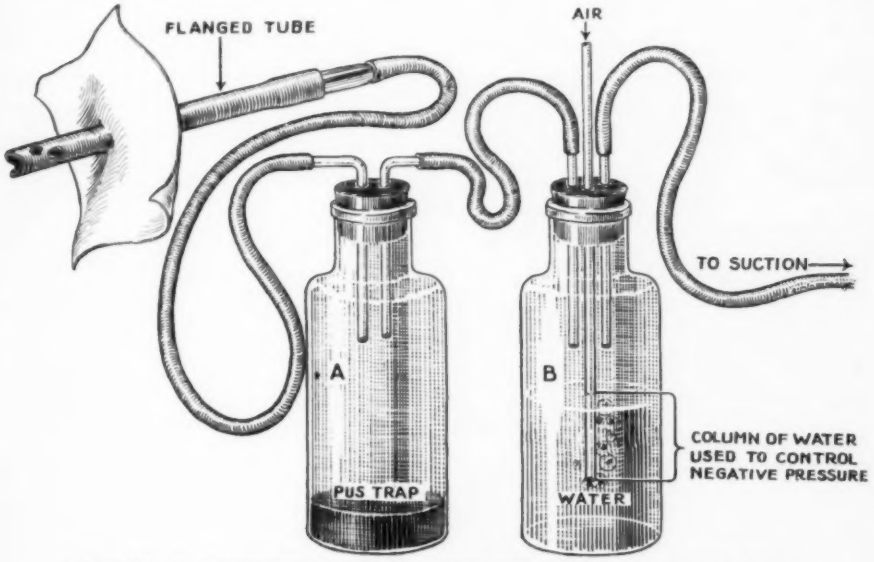

DIAGRAM - I - CONSTANT NEGATIVE PRESSURE APPARATUS WITH PUS TRAP.

Exploration with the finger is often easily carried out, but care is used that parietovisceral adhesions are not broken down. This procedure is not intended to be a wide open exploratory thoracotomy. The special flanged empyema tube is then placed well into the cavity with the intrathoracic part fenestrated. The soft tissues are closed snugly around the tube, the skin is covered with zinc oxide or some similar material and the flanged rubber dam portion of the tube is held in place by firm adhesive strapping to the chest wall. This is held in turn by a many tailed binder so that a firm air-tight dressing is established. The end of the tube is clamped at the end of forced inspiration and the patient is returned to the ward where the tube is connected to the constant negative pressure apparatus. This is simply a tube leading to a bottle serving as a pus trap on the floor. This connects with a similar bottle partly filled with water where negative pressure is maintained by suction and controlled by the simple device shown in the diagram. The main-

tenance of a definite, uniform, continuous suction is a very important feature in the treatment, and this is taken care of by a vacuum pump installed in the basement. This pump with its vacuum chamber is connected by piping to the wards, porches and operating rooms and affords a continuous and unfailing source of negative pressure. The various forms of suction obtained from water pumps, inverted water bottles, etc., we have found unreliable and unsatisfactory.

TABLE III
Comparative Mortality Charts

Operator and hospital	Time	Type operation	No. cases	No. deaths	Per cent mortality
Binney, H. Boston City Hosp.	1928	Closed Few late ops. Open method	126	14	11
Heyer, Y. Johns Hopkins Hosp.	1923	Mixed	425 J. Hop. 30 Cinn. Gen.	62	15.4
Ladd & Cutler Childrens Hosp.	1924	Closed Open Under 2 yrs.	42 226 48		28 15.9 35.5
Hart, Deryl Baltimore	1929	Closed Tidal irrigation	50		10
Graham, E. Barnes Hospital, St. Louis		Closed?	86		11
Brown, Henry P. Childrens Hosp., Philadelphia	1923	Rib resection Intercostal	171 54		21 40
Wilensky, A. O. Mt. Sinai	1903	13 Open and various ops.	225	59	23
Lloyd, Samuel N. Y. Post-Grad.	1907	Open	225	47	20
New Haven Hosp.	1929	Closed suction	153	17	11.1

The post-operative treatment is decidedly easier than that necessary in the usual open thoracotomy. The nurse measures and charts the daily drainage, and checks the apparatus to be sure it is working. This is very simple. The water in bottle B (see diagram) ceases to bubble when the system is plugged or stopped in any way, and with this and the drainage chart a simple but sure check-up of progress is obtained. At the end of the first week the dressing is usually done, the stitches taken out, the tube removed, cleaned and sterilized, shortened and reinserted. This shortening is continued until the pleural cavity is completely obliterated when the apparatus is discarded. Care is taken that the sinus tract in the thoracic wall is kept open until the cavity is completely obliterated. Another important feature in the treatment is that at necessary intervals during the convalescence

the outline of the cavity is mapped out by X-ray after filling with a solution of sodium iodide or some other opaque media, and in this way pocketing or delay in lung expansion is ascertained. Blow bottles are used to help re-expand the lung, and measures directed toward building up the patient's general condition are carried out.

We have not depended upon irrigation with Dakin or other solutions to sterilize the cavity. There have been bronchial fistulæ in this series. Some have delayed convalescence, but they have uniformly closed spontaneously. This type of treatment does not confine the patient to his bed but can be carried out just as effectively with the patient in a wheel chair in the ward or on the porch. An attempt has been made to keep all patients in the hospital until the pleural cavity has been completely obliterated and the sinus tract healed.

RESULTS

This series includes all the cases of post-pneumonic empyemas admitted to the New Haven Hospital* and treated by the staff from 1919 to 1929 with the exception of a few cases admitted late in the disease where the classical open thoracotomy was employed, and two cases treated by the method described, discharged with obliterated cavities but untraceable. There were 153 cases treated by the method described. The first 70 of this group were followed and examined by Beverly Douglas. The last 83 have been followed and examined personally by some member of the Staff with the exception of 7. These have been examined by their family physicians. We do not believe that any case even healed at discharge followed for a short time can be called a cure. We have had many cases treated elsewhere discharged with superficially healed wounds and pronounced cures who have come to this hospital many years later with a recurrent or persistent empyema. One case in our series was followed for two and one-half years. No general or pulmonary symptoms were present and no local signs of disease were noted except those interpreted as thickened pleura. However, three years after his discharge he returned with an empyema necessitatis and a chronic empyema. This case was not checked accurately with follow-up X-rays of his injected cavity, and his sinus tract was allowed to heal before his cavity was obliterated. We believe a superficially healed wound as a measure of cure is a very poor one, and that complete obliteration of the pleural cavity is necessary to prevent recurrence or continuation of the disease.

In the 153 cases there were 17 deaths, a mortality of eleven and one-tenth per cent. In the first 70 cases (followed by Douglas) there were 11 deaths with a mortality of fifteen and seven-tenths per cent. In the last 83 there were 6 deaths with a mortality of seven and two-tenths per cent. Of 36 cases of pneumococcus I empyema, there were 2 deaths, a mortality of five and five-tenths per cent, while in 25 cases in which the streptococcus hemo-

* Dr. Maxwell Lear has reported some of these cases in the Proc. Conn. State Med. Society, May 28, 1924; and Dr. Beverly Douglas has used a few of these cases in a report soon to be published.

lyticus was the infecting agent, there were 3 deaths, a mortality of twelve per cent. There were no deaths at or immediately following operation.

Of these 17 cases, there were 2 where death may have been due to or hastened by faulty application of our method. One, a female child fifteen months old, developed scarlet fever on her fifth post-operative day, was transferred to the Isolation Pavilion and the suction tube was removed. Marked respiratory difficulty with faulty oxygenation and cyanosis, rapid pulse, etc., was followed by death in spite of the rather late administration

TABLE IV
Comparative Chronicity Table

Clinic—operator	Time	Type operation	No. cases	No. chronics	Per cent chronicity
Binney, H. Boston City Hosp., Boston	1928	Closed method Few open method	126	6	4.7
Heuer Johns Hopkins Hosp.	1923	Mixed	425 J. Hop. 30 Cinn. Gen.		20 Some on admission
Ladd & Cutler Childrens Hosp., Boston	1924	Closed Open	42 226		50 4
Hart, Deryl Baltimore	1929	Closed Tidal irrigation	50	0 2 osteo-myelitis	0 4
Brown, Henry P. Childrens Hosp., Philadelphia		Rib resection Intercostal	171 54		47 37
Wilensky, A. O. Mt. Sinai Hosp.	1903	13 Open and various ops.	225		23
Lloyd, Samuel N. Y. Post-Grad. Hosp.	1907	Open	225		Many
New Haven Hosp.	1929	Closed suction	153	1 2 osteo-myelitis	0.6 1.2

of oxygen and an attempt to correct the intrathoracic situation. The other was a seriously ill infant who developed an abscess of the thoracic wall following a diagnostic thoracentesis. The pleura was punctured and an emergency thoracotomy was done far too early in the course of the disease. Pulmonary collapse ensued, which was partly controlled by suction. The wound broke down five days after the thoracotomy and in spite of resuture and reapplication of suction the patient died. In the remaining 15 cases, there were 7 autopsies; pericarditis, mediastinitis and pneumonia were shown to be present in 2 of these 7 cases. Meningitis was present in one, endocarditis with septicemia and pneumonia in 2, bilateral pneumonia and pleurisy

was present in 1 and bilateral pneumonia with multiple abscesses was present in the last. In one of the 8 cases where autopsies were not obtained, the cause of death was a severe pulmonary hæmorrhage from a tuberculous pulmonary lesion. The other 7 presented the clinical picture of an overwhelming infection.

When the deaths are classified according to age, the highest mortality is found in the group under two years, 21.7 per cent, while the lowest mortality is present in those patients between two and twelve years, 5.7 per cent.

In summarizing our mortality, it seems fair to state that in two cases of the 153, death was due to the empyema. But we feel that these deaths were preventable and due to errors on our part. In the remaining 15 fatalities, the cause of death could not be attributed to the empyema per se.

In our statistics relative to the duration of treatment we could not use all of the 153 cases. The choice of the optimum time for operative interference did not rest with us in some of these, because they were admitted to the hospital late in the disease. In others, a definite history of the time of onset could not be obtained and in a few cases, the exact time of complete closure of the sinus tract could not be accurately ascertained because these patients left the hospital before they were entirely healed. However, there are 110 cases with a definite history suitable for statistical study. We have not attempted an accurate estimation of the duration of pleurisy before operative interference for the reason that the exact time of onset is often difficult to state. The average number of days from the onset of the pneumonia until operative interference has been used. With a pneumococcus I empyema, this was 18.7 days, while the average with a streptococcus empyema was 29.5 days. This collaborates the usual clinical experience that a streptococcus pleurisy must be operated late. This figure indeed may be misleading because the onset of the pleurisy is early in a streptococcus infection so that more days of actual pleurisy are present than is apparent from this comparative figure.

The average number of days required before closure of the pleura was 5 days longer with a streptococcus infection. The total average number of days of all cases before operative interference was 24.1 days or just over 3 weeks. The average time for the pleural cavity to become obliterated and closed was 40 days, just under 6 weeks while complete healing required 7 weeks and 2 days; a total period averaging 75 days—10 weeks and 5 days.

Regarding the third feature of our consideration, chronicity, two cases have had osteomyelitis of the ribs and have required secondary operations for the removal of infected bone. One case operated upon very early after the onset of a pneumococcus empyema had a bronchial fistula, a partial collapse of the lung and required 118 days before his pleural cavity was obliterated and his sinus tract healed. One case previously mentioned discharged before complete obliteration of cavity returned three years later with a chronic empyema. We have regarded any instance where a secondary operation was necessary as a chronic empyema. We have three in this group, two of these with

obliterated empyema cavities but with osteomyelitis of the ribs. The pleural cavity has been obliterated without operative interference and remained so in all cases except the one mentioned. It is interesting to note that in this series of cases there were two with a bilateral empyema, both received bilateral drainage and were treated with the usual suction tube drainage, and both cases healed rapidly and without complications. There was also one case of acute suppurative pericarditis occurring in a patient already undergoing treatment for his empyema where the pericardial cavity was drained and both cavities healed well without complications or sequelæ.

SUMMARY

A brief resume of the present physiological and pathological concepts underlying the treatment of acute suppurative pleurisy is followed by a description of the method of treatment used in the New Haven Hospital.

TABLE V

Duration of Treatment—Only Cases Admitted to Hospital Early in Disease

Organism	No. cases	Average no. days from onset pneumonia to oper.	Average no. days from onset pneumonia until pleura closed	Average no. days from onset pneumonia for complete healing
Pneumococcus Type I	30	18.7	39.3	49.3
Pneumococcus, all other types	24	24.1	42.7	54.5
Hemolytic streptococcus	24	29.5	44	56.7
Non-hemolytic streptococcus	5	28.6	30.7	42.5
Staphylococcus {Aureus / Albus}	5	17.8	47	58.7
Unknown and Mixed	22	24.2	38.8	47.8
Average all types	110	24.1	40.6	51.3

Essentially this is thoracentesis, delayed partial costectomy and constant suction tube drainage.

Results obtained in 153 cases of post-pneumonia empyema treated by this method are charted and discussed regarding mortality, length of convalescence and chronicity, with the various types of infecting organisms, and as a whole. Of the 17 deaths, 2 were due to the empyema, but both of these should have been prevented. The other 15 deaths were due to overwhelming infections and complications. The average length of treatment in this series was three weeks from the time of the onset of the pneumonia until operative interference, just under six weeks from the onset for obliteration of the empyema cavity and just over seven weeks for complete healing. There were two cases of osteomyelitis in this series. There was one instance in which the pleural cavity was not obliterated due to faulty post-operative care.

CONCLUSIONS

One hundred and fifty-three consecutive cases of post pneumonic empyema are reported, treated by delayed costectomy and constant suction tube drain-

age, with uniform and complete obliteration of the empyema cavity except in one case. From study of this series we believe it fair to assume that:

1. Death should never result from empyema thoracis per se.

2. Chronic empyema should not occur in properly treated cases of acute suppurative pleurisy.

3. The basis of the determination of a cure should be the disappearance of all signs of sepsis, a complete obliteration of the empyema cavity as well as a healed superficial wound, and a long time follow-up.

I wish to express my indebtedness to Dr. Samuel C. Harvey for his valuable criticisms and suggestions.

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A BACTERIOLOGICAL AND CLINICAL STUDY OF GASTRIC ULCER*

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THIS REPORT WAS AIDED BY A GIFT FROM MRS. JOHN L. GIVEN IN SUPPORT OF SURGICAL RESEARCH

This investigative work here reported has been made possible by the collaboration of the Department of Surgical Research, the Second Surgical Division (Bellevue) and the Department of Public Health and Preventive Medicine of Cornell University Medical College and respectively directed by Dr. Joshua E. Sweet, Dr. Harold Santee, Dr. John C. Torrey and Dr. Morton Kahn.

The study involves a bacteriological and clinical investigation of gastric, duodenal and gastro-jejunal ulcer, the results of which support the theory that their etiology is due to a specific infection.

Etiological theories other than infection may be grouped under four headings; namely:

1. *Vascular.*—Resulting from a deficient blood supply to the gastric mucosa.
2. *Toxic.*—Resulting from the action of toxic agents.
3. *Neurologic.*—Resulting from trophic and glandular disturbances.
4. *Chemical.*—Produced by the action of the digestive juices.

The vascular theory is supported by the fact that intravenous injections of material causing emboli, ligation of more than one-third of the blood supply to the stomach, the injection of drugs causing spastic contraction and local ischæmia, with resulting local areas of anæmia, and ligation of the portal vein, or an Eck fistula in dogs, ulcers of the stomach will be produced inconstantly. Prolonged starvation will do the same.

Because of the fact that lesions of the stomach resembling ulcer result when toxic drugs and chemicals are injected locally or generally, and that similar lesions are produced when biologic toxins, foreign protein, dead bacteria, filtrates of living bacteria, gastro-toxic serums, hepatotoxin, enterotoxin and extracts of burned tissue, the toxic theory originated and survives.

When the spinal cord, anterior corpora quadrigemina, median splanechnic nerves or vagi are sectioned, ulcer results inconstantly, and likewise when the celiac plexus is extirpated. Lesions of the suprarenal glands occur following nerve section. Removal of the adrenals without nerve section is sufficient to cause ulcers to form. These factors support the trophic and glandular theory.

Leriche has lately asked the question, "How could ulcers, so large and adherent that their resection was technically impossible, heal so rapidly fol-

* Read before the Philadelphia Academy of Surgery, April 7, 1930.

lowing gastroenterostomy or simple excision if they were trophic in origin? How could resected stomachs heal so well in patients who have had an ulcer for a great number of years, if there was any trophic disturbance of the stomach?"

Gandier[5] has lately cited a case in whom a deinervation of the stomach was done because of ulcer symptoms but no ulcer was demonstrable at the time of operation. Less than a year later the patient was reöperated upon for a perforated gastric ulcer which developed after deinervation.

That these three methods of experimental approach will inconstantly produce ulcers in the stomach of the animal is true. That they have the characteristic feature of the human ulcer, namely, chronicity, is not true.

The only experimental method which has consistently produced ulcers in the pyloric region of the stomach of the dog comparable to those found

PLATE I

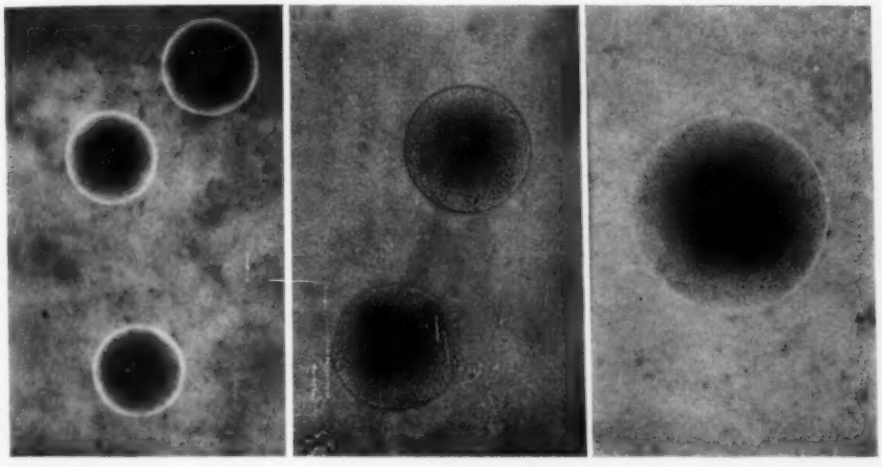

FIG. 1.—All S colonies culture 63.

FIG. 2.—All S colonies culture 68.

FIG. 3.—First appearance of O intermediate change. Culture 64.

in man has been that of surgical duodenal drainage which mechanically brings about a disturbance of the acid and alkali (or bile), at the pylorus. The ejected acid stream from the stomach strikes a loop of anastomosed jejunum unprotected by alkaline duodenal contents. Chronic ulcers result which can later be healed by reintroduction of alkali (bile), by gastrojejunostomy and pyloric exclusion protecting the ulcer from acid chyme. This work originally done by Mann and Williamson[1] and corroborated by Morton,[2] McCann, and lately Weiss[4] is beyond experimental error. There can be no question, therefore, that normal duodenal contents have some protective action preventing the formation of an ulcer. This is strengthened by the fact that tying off the common duct causes ulcers to form in the duodenum inconstantly, and that ulcers have formed following chronic biliary fistulæ in humans.

Mechanical and anatomical factors may play a rôle. The duodenum is

the region of greatest fixation and the poorest and most tortuous blood supply. The normal protecting rugæ of the mucosa are sparse or absent at the pylorus and the mucous membrane of the duodenum is extremely friable. The muscular activity of the antrum and valve itself, which is easily thrown into severe contraction and spasm from irritation as one observes experimentally, plays a rôle.

As will be indicated later, the pertinent anatomical relationship may be with the biliary passages rather than with the above-stated factor, and equally important may be the functional mechanism which makes possible regurgitation into the first portion of the duodenum and stomach of alkaline duodenal contents rather than the passage out from the stomach of acid contents.

The ulcer patient is invariably of the asthenic type with a narrow costal

PLATE II

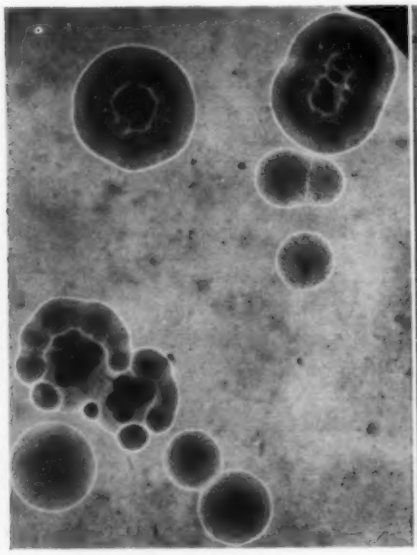

FIG. 4.—S and O colonies. Culture 60A.

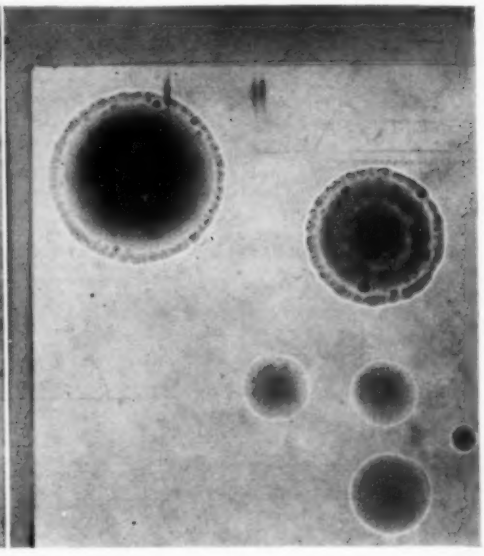

FIG. 5.—S and O colonies. O colonies showing ring of daughter colonies. Culture 59A.

angle, and similar sharp duodenal angle which anatomically should hinder bile regurgitation into the first portion of the duodenum.

The theory that gastric ulcer has an infectious origin is as old as the first anatomical description of ulcer. Investigators in every decade for the past 100 years have brought forward evidence to prove its infectious origin. The literature has been completely reviewed in a previous article.[3]

The following investigative results are offered to again support this theory.

1. Pathological investigation of immediately prepared resected specimens reveals typical inflammation, showing zones of exudation, fibrinoid necrosis, granulation and cicatrization. The exudation may be purulent, fibrino-purulent or catarrhal. Granulation tissue is variable in extent and is not different from granulation tissue elsewhere. When fresh specimens were fixed immediately and stained by the method of Levaditi, a rim of strepto-bacilli was always present covering the necrotic surface of the mucous mem-

brane. Single cocci, diplococci, strepto-bacilli and rods were constantly present in the exudate which forms the surface of the ulcer. Phagocytic white cells showing large stained granules were numerous in the sanguino-exudate. The organisms were practically never found below the submucosal layer. If the base of the ulcer was a cicatrized muscle layer, the mucosa being entirely destroyed, no organisms were found. The glands of the mucosa adjacent to the exudative necrotic crater would invariably show organisms and beginning destruction. The mucosa not adjacent to the crater appeared normal and the rim of organisms on the surface stopped. Although definite thrombosis of vessels is noted microscopically, it could better be explained as an antecedent rather than a precedent factor. A few slides have shown organisms in the thrombosed lumen.

TABLE I

Sources of single colony strains from stomach

Patient	Hospital – Surgeon	Ulcer	Single Colony Strains
1. Male	Second Surgical Bellevue Santee	Large gastric lesser curvature	1. A′ 3. A. 2. A 4. A
2. Male	Second Surgical Bellevue Santee	Small gastric lesser curvature	19. AA′ 21. AA′ 20. A 22. A
3. Male	Second Surgical Bellevue Santee	Small gastric lesser curvature	23. A 23b. A 23d. A 23a. A 23c. A 23e. A
4. Male	Second Surgical Bellevue Santee	Carcinoma ulcer mid-stomach	45. A 45b. A 45d. A 45a. A 45c. A 45e. A 45fA
5. Male	Mount Sinai 300520 Berg	Duodenal	46. A 46a. A 46b. A.
6. Male	Mount Sinai Private Patient—Berg	Large gastric lesser curvature	47a. A 47b. A. Eight strains
7. Male	Mount Sinai 300854 Berg	Large gastric lesser curvature	53. A 53b. A. 53d. A 53a. A 53c. A.
8. Male	Second Surgical Bellevue Dudley	Gastrojejunal	55. A 55b. A 55d. A 55a. A 55c. A
9. Male	Second Surgical Bellevue Dudley	Gastrojejunal	56. A. 56a. A.
10. Male	Second Surgical Bellevue Dudley	Large gastric lesser curvature	58. A′.
11. Female	Second Surgical Bellevue Santee	Two prepyloric ulcers, carcinoma	59. A 59. A′
12. Female	Second Surgical Bellevue Santee	Prepyloric ulcer, carcinoma, Metastases	60. A 60. A′
13. Male	Second Surgical Bellevue Santee	Large gastric pars media	61. A′
14. Male	Second Surgical Bellevue Santee	Large gastric perforated, pars media	62. A′
15. Male	Second Surgical Bellevue Santee	Gastric ulcer lesser curvature	63. A′
16. Male	Second Surgical Bellevue Santee	Perforated duodenal ulcer	64. A′

TABLE I—*Continued*

Patient	Hospital-Surgeon	Ulcer	Single Colony Strains
17. Male	Second Surgical Bellevue Santee	Prepyloric ulcer polypoid carcinoma	66. A′ 66. B.
18. Male	Second Surgical Bellevue Santee	Duodenal healed gland lesser curvature	67. A′
19. Male	Second Surgical Bellevue Santee	Large prepyloric ulcer	68. A′

A—Viridans—slight hemolysis
A′—Viridans—marked hemolysis
AA′—degree between A and A′
B′—complete hemolysis

This classification is based upon the degree of hemolysin produced by the organism. It seems, however (see text), that this hemolysin production is variable. It appears to be lost when the organism shifts from the S to the R type, but this point must be investigated in detail before it is accepted in its entirety. If such proves to be the case, however, it would seem that a reconsideration of classification of the streptococci on the basis of hemolytic activities would be necessary.

1928–1929

TABLE II

Agglutination and absorption table

(*a*) *Agglutination with serum 2*

Antigens	1–100	1–200	400	800	1600	3200	6400	12800	Control
Gastric 2	#	#	#	#	#	+|	+	±	–
Gastric 20	#	#	#	#	#	+	±	|	–
Gastric 23	#	#	#	#	#	+|	+	±	–
Gastric 45	#	#	#	#	#	+	±	|	–
Gastric 47	#	#	#	#	#	+|	±	±	–
Gastric 53	#	#	#	#	#	+|	+	|	–
Gastric 55	#	#	#	#	#	+	±	|	–
Gastric 56	#	#	#	#	#	+	±	|	–
Gastric 9	#	#	#	#	#	+	±	–	–
Throat 29	#	#	#	#	#	+|	+	|	–
Throat 38	#	#	#	#	#	+	±	|	–
Throat 39	#	#	#	#	#	+|	±	|	–
Throat 44 A	#	#	#	#	#	+	±	|	–
Gastric 58	#	#	#	#	#	+|	±	|	–

(*b*) *Absorption of serum 2*

Antigens	1–100	200	400	800	1600	3200	Control
Gastric 2	–	–	–	–	–	–	–
Gastric 20	–	–	–	–	–	–	–
Gastric 23	–	–	–	–	–	–	–
Gastric 45	–	–	–	–	–	–	–
Gastric 46	–	–	–	–	–	–	–
Gastric 47	–	–	–	–	–	–	–
Gastric 53	–	–	–	–	–	–	–
Gastric 55	–	–	–	–	–	–	–
Gastric 56	–	–	–	–	–	–	–
Gastric 9	–	–	–	–	–	–	–
Throat 29	–	–	–	–	–	–	–
Throat 38	#	+	|	–	–	–	–
Throat 39	–	–	–	–	–	–	–
Throat 44 A	#	#	+	±	–	–	–

TABLE II—*Continued*

Lip ulcer strain from penetration of tooth—Serum 40

Antigens	1–100	1–200	400	800	1600	3200	6400	12800	Control
Lip ulcer 40	#	#	#	#	+|	+	±	|	–
Teeth 15	#	#	+|	+	|	–	–	–	–
Teeth 17	#	#	+|	±	–	–	–	–	–
Lip ulcer 31	#	#	#	+	|	–	–	–	–
Hand ulcer 7	#	#	#	+|	±	|	–	–	–
Hand ulcer 11	#	#	#	+	±	|	–	–	–
Hand ulcer 30	#	#	#	±	|	–	–	–	–
Gastric 2	#	#	+|	+	±	–	–	–	–

Note.—For all methods of technic, see previous article.[3]

\# indicates complete agglutination—fluid clear
+| indicates nearly complete agglutination—slightly cloudy and fluid clumps smaller
\+ indicates 50 per cent complete
± indicates slightly less than 50 per cent
| indicates trace of agglutination

1929–1930

TABLE III

Agglutination table—Agglutination with Serum 66

Antigens	1–100	1–200	400	800	1600	3200	6400	12800	Control
Gastric 66	#	#	#	#	#	+|	±	–	–
Gastric 58	#	#	+|	+	+	|	–	–	–
Gastric 59A	#	#	#	#	+|	+|	|	–	–
Gastric 59A′	+|	+|	+|	+|	+	+	|	–	–
Gastric 60A	#	#	#	#	+|	±	|	–	–
Gastric 60A′	#	#	#	#	#	+	±	–	–
Gastric 61	#	#	#	#	+|	+|	±	–	–
Gastric 62	#	#	#	+|	+|	+	±	±	–
Gastric 63	#	#	#	#	#	+|	±	–	–
Gastric 64	#	#	#	#	#	+	|	–	–
Gastric 67	#	#	#	#	#	+|	–	–	–

Absorption table—Absorption of Serum 66

Antigens	1–100	1–200	400	800	1600	3200	Control
Gastric 66	–	–	–	–	–	–	–
Gastric 58	–	–	–	–	–	–	–
Gastric 59A	–	–	–	–	–	–	–
Gastric 59A′	–	–	–	–	–	–	–
Gastric 60A	–	–	–	–	–	–	–
Gastric 60A′	±	–	–	–	–	–	–
Gastric 61	–	–	–	–	–	–	–
Gastric 62	–	–	–	–	–	–	–
Gastric 63	–	–	–	–	–	–	–
Gastric 64	–	–	–	–	–	–	–
Gastric 67	±	–	–	–	–	–	–
Gastric 68	+	±	–	–	–	–	–

Note.—Strain 68 proved identical by absorption. Last culture obtained and not yet homogenized for cross agglutination.

Series 1929–1930 identity with Series 1928–1929 proved by Strain 58.

2. A green-producing streptococcus which can be classified as an alpha or alpha prime type, depending upon its stage, which will be referred to later, has been cultivated from nineteen resected gastric, duodenal and gastrojejunal ulcers and proved to be an agglutinogenic and antigenic homolog by differential cultural tests and by agglutination, cross agglutination and agglutinin absorption.

Four partially healed duodenal ulcers and one gastric ulcer in patients in whom a gastroenterostomy was present gave sterile cultures. Other organisms grown inconstantly were the B. welchii, B. coli, a gamma enterococcus, Opler-Boas bacillus, a Gram-negative diplococcus resembling one of the throat organisms described by Elser and Huntoon and a Gram-negative chained bacillus. The last four were only present in five of the largest gastric ulcers which were both macroscopically and microscopically cancer.

Ten of the cultures gave a pure growth of the alpha streptococcus.

Normal stomach wall gave repeatedly negative cultures except for a gamma enterococcus and B. coli.

By the same methods the gastric alpha streptococcus strain has been shown to have agglutinogenic and antigenic identity with four alpha strains cultured from the lesions of four cases of an acute specific disease characterized by small ulcers of the lip, tongue, buccal membranes and tonsils. It has been shown to have a relationship but not to be identical with alpha prime strains producing ulcers of the skin but not to be related to alpha strains from teeth and tonsillar foci of patients suffering with gastric ulcer or with gamma strains isolated from appendicitis and cholecystitis.

TABLE IV

Ulcer series

Agglutination of Serum of Patients with Proved Gastric Ulcer with Antigens of Various Gastric Strains

Agglutination Titre	Number of Patients
1–1280	3
1–160 or 320	46
1–80	63
	Total 112

Control series

Serum of Patients with Varied Types of Streptococcus Infections

Agglutination Titre	Number of Patients
1–40 or less	40

Ulcer Patients Serum Following Vaccine Therapy with Organism in Avirulent Stage *

Agglutination Titre	Number of Patients
1–10 and no agglutination	11

* *Note.*—The vaccine was made when the organism was in its avirulent O and R type (see text). It therefore did not excite agglutinin formation, but the ulcer must have become less active to show a reduction or absence of the agglutinins present before vaccine therapy. Vaccine has now been prepared from the organism in its S virulent stage.

3. The blood serum of 112 patients suffering with gastric, duodenal or gastrojejunal ulcer has shown a specific agglutination against the antigen of the gastric strain ranging in titre from 1–80 dilution to 1–1280. Control serum from patients suffering with other types of streptococcus infections has never shown agglutination in titre above 1–40. A

control serum was run with every test as well as a great number from patients suffering from streptococcus cellulitis, acute infectious arthritis and erysipelas.

The highest titre agglutination occurred in serum obtained from patients with perforated or bleeding ulcers, with less high titres in serum from patients who were under treatment, whose symptoms were minimum and whose ulcers were comparatively inactive, but always a higher titre than any control. It has so far been 100 per cent. perfect from the standpoint of diagnosis.

Furthermore, eleven patients from the Cornell Clinic, previously untreated, showing positive X-ray evidence of duodenal ulcer and whose blood serum showed a high titre agglutination, had the titre of the control serum agglutination at the end of a two months' course of vaccine from the gastric streptococcus. The vaccine contained two billion killed organisms to the cubic centimetre, the dosage consisting of 0.2 cubic centimetre to two cubic centimetres increasing every five days by 0.2 cubic centimetre. Their symptoms had completely subsided, but by X-ray their defect still remained. Medical

PLATE III

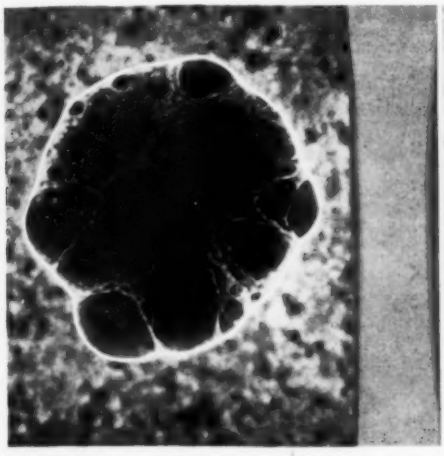

FIG. 6.—Last O stage. Most of colony in the R stage. Very little S element left. Culture 47B.

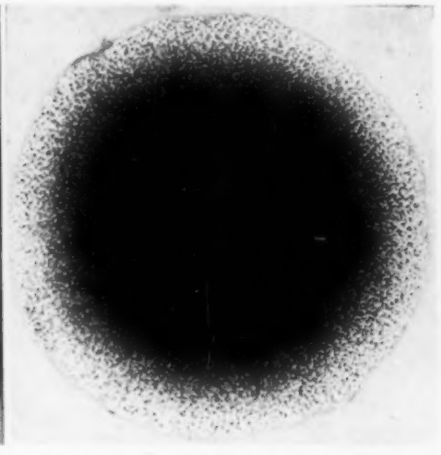

FIG. 7.—Complete stable colony. Culture 2.

treatment will do as well. Only over a longer course of time eliminating recurrences can any benefit be claimed.

4. Experimentally, it is not possible to produce an ulcer in the stomach of a dog by a single injection of a culture of the gastric streptococcus by any method used. Its pathogenicity, however, is illustrated by its ability to produce a small ulcer in the skin of the dog following intradermal injection. Injection beneath the skin has no effect.

Allow for a minute a brief résumé of the bacteriological difficulties encountered which have been known to all investigators since the original work of DeKruif on the phenomenon of dissociation. It has been witnessed by a number of observers working with a large variety of organisms and is now accepted as a phenomenon widely distributed in nature, concerning the validity of which there is no question. A remarkable summary of the entire problem has lately been made by Hadley.[6]

It is extremely important, however, for the same thing may happen in the human body and is the result of favorable or unfavorable environment, especially p^H.

Although a single cell study has not yet been made, the difficulties encountered in this investigation, which has been a single colony study, would suggest that it is entirely due to this phenomenon of dissociation and not because more than one strain was present, or that it is due to contamination of cultures, or an evaporation phenomena, the latter

of which has been disproved by comparison of growth under constant conditions of moisture.

With the gastric strain the hæmolytic, antigenic and agglutinogenic reversals arise as the S (smooth) type changes to the R (rough) type of colony growth and O (intermediary) types under the influence of age and method of cultivation. When the organism was first recovered alpha prime hæmolysis was always present and in one case beta hæmolysis was present. After the second or third generation under the conditions of artificial cultivation, O and R forms become more prevalent and there is no hæmolysis even though *identical* blood plates are always used.

Antigenic and agglutinogenic power diminishes when colony growth reaches the intermediary O stage and vanishes with the R stage. The centre of an O colony shows many dead organisms, the edge daughter colonies living.

A lactose purple agar plate will show evidence of extremely active fermentation when the organism is in the complete R stage and only slightly when in the S stage.

The organism when in the S stage is virulent, for extremely small graded doses of a living culture are necessary to build up the titre of rabbits' serum because larger doses kill, while huge intravenous doses of the live culture in the R stage will not affect the rabbit nor can a serum titre of any degree be obtained. It has been demonstrated with other organisms that phagocytosis occurs only when these organisms are in the R stage.

Morphologically, the organism varies in each stage. Single and diplococci with few chains are noted in the S stage, short and long chains in the intermediary stages and small clumps in the R stage. The organism morphologically closely resembles the enterococcus in the R stage but there is always marked greening and never has it become a gamma type. The organism has consistently fermented lactose, sucrose and salacin and other sugars only rarely. This factor, besides its inability to grow on whey agar, distinguishes it from the commonly found enterococcus.

When an O (intermediary) culture is transplanted daily in 10 per cent. ox bile broth it rapidly reaches the stable R stage. Media of lactose agar to which human bile from an ulcer patient has been added shows no growth with S phase when the amount is more than one cubic centimetre of bile to fifteen cubic centimetres of media. The organism in its S stage will not grow in bile broth media of the lowest dilutions no matter how many times it is replanted. Bile, therefore, must have some protective substance which has the ability to prohibit the growth of the S organism and to keep the O and R organisms in a non-virulent state. It is known that bile salts kill pneumococci. Whether it is this factor with the gastric streptococcus or a vitamin content of the bile would be difficult to say. This phase of the problem is now being investigated.

A patient who had had a gastroenterostomy for a proved duodenal ulcer and who was later reöperated upon for a marginal ulcer, at which time the gastroenterostomy was undone and the marginal ulcer not demonstrated, again came to operation for positive X-ray diagnosis of duodenal ulcer. The duodenal ulcer, however, could not be demonstrated after cutting into the stomach. There were two large glands on the lesser curvature which were cultured. The alpha streptococcus was recovered and when first plated was in the complete R stage. This supports the belief that the same thing happens *in vivo* as *in vitro* for the ulcer was healed but the organism was there in its non-virulent form.

The clinical aspect of ulcer is well known. It runs truer to anthropological type than any other disease; it is definitely seasonal; it is chronic; it closely follows the course of other chronic infectious diseases in its characteristic periods of quiescence and recurrences over a long period of time; an excellent comparison is offered by osteomyelitis.

Experimentally, the only method by which ulcers have been produced

comparable to those found in man has been by the method of surgical duodenal drainage.

It is possible that the protective substance in bile, whatever it may be, has been removed and a normally non-virulent organism in its R stage becomes S and virulent. Attempts are now being made to maintain the stability of the S type and to reconvert the R type back to its S type, as Dawson[8] has done with the pneumococcus.

One can only surmise in the ulcer patient whether there is something deficient in their bile or whether there is not enough bile for protection. Failure of regurgitation of bile into the first portion of the duodenum and stomach may be at fault, due to the sharp duodenal angle.

Women suffer from ulcer rarely and then usually in combination with gall-bladder disease.

It is a common occurrence to have a previous duodenal ulcer recur when a gastroenterostomy previously performed for its cure is unhooked because of recurrent symptoms but no ulcer demonstrable.

The operations giving the most satisfactory results are those in which the bile is mechanically put back into the stomach, and four duodenal and one gastric ulcer, in patients in whom a gastroenterostomy was present, have given the only negative cultures.

There are over one hundred reported cases of perforated duodenal ulcer in marasmic babies from one to six months of age. Helmholz[10, 11] has demonstrated the infectious origin in many of them. They certainly do not have any foci of infection but they could be deficient in the physiology of their bile which prohibits the growth of the gastric streptococcus.

It has previously been stated that five of the ulcers, or 26 per cent., of the series of nineteen had undergone malignant degeneration. The organism's marked degree of transforming glucose into lactic acid has been noted. Because of the work of Otto Warburg[7] on lactic acid formation by the tumor cell, accurate analysis of the exact amount of lactic acid formed by the organism was done by the Laboratory of the Russell Sage Institute under the supervision of Doctor Shorr. The method used was that of Friedemann, Shaffer and Cotonio.[12]

R strain 64 and R strain 68 in 0.1 per cent. glucose broth containing 7.3 milligrams of glucose, in a twenty-four hour growth produced .59 and .68 milligrams of lactic acid, which shows that from 80 to 93 per cent. of the glucose was transformed into lactic acid by the organism.

A comparison of lactic-acid production by R strain 64 and S strain 68 in 1.0 per cent. glucose in a twenty-four hour growth showed that out of the 75 milligrams of glucose present, R 64 produced 3.37 milligrams of lactic acid, and S 68, 1.53 milligrams or approximately 4.5 and 2.1 per cent. respectively. Therefore lactic acid produced by the R strain is 100 per cent. greater than that produced by the S strain.

The 0.1 per cent. dilution of glucose approximates the glucose content of the blood and a greater degree of glycolysis resulted than with the 1.0

per cent. dilution which contained more glucose than the amount of growth of the organism could reduce.

Because the organism grows best under anærobic conditions, its energy probably is derived from glycolysis and very little from oxygen consumption. This is the type of metabolism of the carcinoma cell.

Part of the lactic acid found in the stomach contents in carcinoma of the stomach could be due to these organisms.

It is possible that the lactic acid produced by the organism in the ulcerated lesion may be a source of constant irritation to the tissue which may, after a long time, cause a transformation of normal into carcinomatous tissue as a number of the irritants are able to do, or possibly prepare the normal cell with lactic acid which Bierick, quoted by Warburg, believes is necessary for the spread of carcinoma.

Although lactic acid is formed by other intestinal organisms they do not produce lesions and therefore are not a source of irritation to the tissue. In muscle and retina, *etc.*, the lactic acid formed is buffered by good blood supply making neutral sodium lactate. A chronic ulcerated lesion has extremely poor blood supply and poor lymph return. The normal p^H of the tissue is also altered in the chronic lesion, also any buffer present might be exhausted by the Hcl. of the stomach.

Further investigation of this problem is now being carried on.

SUMMARY AND CONCLUSIONS

A summary of the facts which favor an infectious etiology of ulcer of the stomach are:

1. A streptococcus has been isolated from nineteen resected gastric, duodenal and gastrojejunal ulcers and proved to be identical and specific by differential cultural tests and by agglutination, cross agglutination and agglutinin absorption.

2. Its agglutinogenic and antigenic identity with similar strains producing ulcers of mucous membrane and skin has been demonstrated and likewise its non-identity with strains from foci of infection and appendicitis and cholecystitis has been shown.

3. Patients suffering from gastric ulcer have this organism's specific agglutinins in their blood serum in 100 per cent. of cases tested, while those suffering from any other type of streptococcus infection fail to agglutinate it or only in low titre.

4. The organism is apparently present in the lesion in immediately prepared Levaditi tissue sections.

5. The organism undergoes dissociation S (virulent) to R (non-virulent) under artificial cultivation and the possibility of it doing likewise *in vivo* has been demonstrated.

6. The S (virulent) form will not grow in bile in low dilutions and the O (intermediate) form rapidly becomes R (non-virulent) under bile cultivation.

7. Surgical procedures which return bile to the ulcer-bearing area give the best clinical results.

8. The marked degree of lactic-acid formation by this streptococcus has been noted and its relationship to carcinomatous degeneration suggested.

The department wishes to thank Dr. Robert Felter and Dr. William Hinton for their coöperation, and also the First Surgical and Second Medical Divisions of Bellevue Hospital and the Cornell Clinic, 16 E. 90th St., New York City.

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ACUTE ULCERATIONS OF THE STOMACH IN CHILDREN

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Acute, fatal ulcerations of the stomach in children are sufficiently rare to warrant the report of the following case, with a review of the literature of the condition.

Case Report.—C. C., female, aged twenty-two months, was admitted to The Babies Hospital January 26, 1930, with the complaint of frequent vomiting during the previous thirty-six hours. She was the only child of young and normal parents. She was a full-term baby, vertex presentation, and weighed seven and one-half pounds. The history failed to disclose any past serious illnesses, injuries or operations. There were no abnormal symptoms referable to the stomach or duodenum.

Present illness.—Two days before admission the child was slightly flushed and seemed feverish although she continued to be playful and ate well. At night, however, she was restless. The day before admission, she started to vomit and refused to take food. All fluids given by mouth were immediately vomited. The vomitus was always watery and never contained blood or fecal material. The baby slept poorly and was very restless although the mother thinks that the child had no fever. On the day of admission the mother noticed that the child's abdomen was swollen and tender but she never complained of abdominal pain. There had been no defecation for two days. An enema the night before admission and another on the day of admission gave small fecal returns. For several days the baby had had a running nose but there were no other symptoms of an upper respiratory or pulmonary infection. There were no genito-urinary symptoms.

Subsequent questioning of the father revealed the fact that three or four days before admission the child was playing with a glass bottle which broke. When the parents tried to assemble the pieces it was found that a small portion was missing. The baby had the habit of putting all sorts of things in her mouth and it is the belief of the parents that she may have swallowed this missing piece of glass.

The patient was a well-developed and well-nourished female of twenty-two months. The skin was pale, cold and dry. The eyes were sunken. She was restless, picked at the bedclothes, and pulled at her mouth and throat. The respirations were labored and grunting but not rapid. The legs were drawn up at the hips. The head, neck, lungs and heart showed no important abnormalities. The pulse rate was 200 per minute. The abdomen was very full and distended and small dilated veins were present over the upper part. The liver dullness was completely obliterated. The liver and spleen were not palpable and no masses could be felt. There was marked dullness in both flanks and above the pubis and this dullness shifted with change of position. A fluid wave was present. No localized tenderness could be elicited although palpation seemed to cause pain. The external genitalia were normal. Examination by rectum revealed no masses or tenderness. The patellar reflexes were normal.

The respirations were 24 per minute and the admission temperature was 99.6°F. The white blood corpuscles were 8,400 per cubic millimetre, and showed 60 per cent. polymorphonuclear leucocytes, 38 per cent. small lymphocytes and 2 per cent. large mononuclears.

A milk and molasses enema given shortly after admission showed a small fecal return.

The diagnosis of peritonitis with possible ruptured viscus was made and laporatomy was decided upon. Under novocaine anæsthesia, a right rectus incision was made and the abdominal cavity opened. A quantity of air, together with about 2,500 cubic centimetre of fluid, escaped. The fluid was dark brown in color and contained numerous food particles, curds of milk and globules of oil. The peritoneum was everywhere injected but there was no purulent exudate. The small intestines and colon were collapsed and contracted. The appendix was normal except for peritoneal injection. The lesser peritoneal cavity was bulging with undigested food.

The child ceased breathing during the exploration of the abdomen. The anterior stomach wall was opened and a perforation about three centimetres in diameter was found on the posterior wall of the fundus. The edges were ragged, soft, frayed-out and deeply hæmorrhagic. No foreign body was found. Sections for microscopic study

FIG. 1.—Photograph of a portion of the stomach. On the upper border is a part of the ulcer, showing the thin, hæmorrhagic and frayed-out edges.

FIG. 2.—Photomicrograph of a section taken from the border of the ulcer at operation. Necrosis of the epithelium, together with œdema and marked polymorphonuclear infiltration of the submucosa is shown. The vessels contain fresh thrombi.

were cut from the edge of the perforation and fluid from the peritoneal cavity was saved for chemical analysis.

"The *autopsy* was done by the medical examiner who found nothing pathological in the heart and lungs. The peritoneal cavity contained a large quantity of fatty fluid with kernels of yellow corn. The stomach showed a round hole five centimetres in diameter in the posterior wall near the fundus (Fig. 1). Surrounding the ruptured area there was a dark red hæmorrhagic zone, but beyond that the mucosa was apparently normal. No foreign body was found in the stomach, intestines or abdominal cavity. The intestines were normal throughout and no blood was present. The liver was moderately fatty. The spleen weighed eighty grams. It was enlarged, firm, with prominent Malpighian bodies. The thymus was not enlarged. It weighed twelve grams.

Microscopic examination of a section which included the hæmorrhagic edge of the tear and a narrow adjacent area of gastric wall (Fig. 2), which appeared to be normal, revealed necrosis of the mucosa; swollen, œdematous submucosa in which lay several thrombosed vessels. In the adjacent area of mucosa thrombosed capillaries were present

between the glands which were in various stages of disintegration, merging into a normal mucosa. The muscle coats were œdematous and infiltrated with polynuclear leucocytes which were also present in large numbers around congested blood-vessels in the submucosa. A fold of mucosa with normal glands showed œdema of its submucosa and congestion of its vessels extending beyond the area of thrombosis.

Another section taken at the medical examiner's autopsy showed a fibrinous exudate on the serosa and polynuclear infiltration of all the coats with marked œdema and a fairly well-maintained mucosa.

This looks like an acute ulcer with secondary inflammation of the gastric wall, although the presence of a previous gastric lesion cannot be excluded." (Dr. Martha Wollstein)

The subject under discussion is acute ulceration of the stomach in children under ten years of age. By ulceration we mean a destructive process which involves not only the mucosa but also a portion of the submucosa and muscularis and which in certain instances may progress so as to involve the serosa. Erosions on the other hand never extend beyond the mucosa. It is this question of depth which separates the erosions and the true ulcers into two large and distinct groups.

Ulcers can further be divided into those which are acute and those which tend to run a chronic course. The acute ulcers are sudden in onset, produce marked and often alarming symptoms in previously supposedly well children and progress rapidly, either to healing or to perforation. Severe hæmorrhages are common.

The chronic ulcers of childhood are entirely different. They are similar pathologically to the ordinary chronic ulcers of adult life and also give rise to the same group of chronic but often more mild gastric symptoms. These chronic ulcers of childhood show the same indurated, infiltrated and sharp edge which is typical of those of adult life. The base is often composed of only a thin layer of muscle and serosa and perforation is not uncommon. The latter, however, differs from the perforations of the acute ulcers in that it is usually small and is situated in the center of a well-formed crater. In this paper, chronic, indurated gastric ulcers of childhood will not be discussed.

Etiology of acute ulcers.—Hæmorrhagic erosions of the mucosa and acute ulcerations of the stomach wall have long been considered to be closely related conditions. In both there is a local disturbance of circulation which in the true erosion is limited to the mucosa. In the ulcerative process, the vascular lesion extends deeper and involves the underlying layers of the stomach wall. To this disturbance of circulation is added complete or partial digestion of the infracted area. The sequent of events, therefore, in acute ulceration of the stomach is hæmorrhage, followed by gastric digestion. Because of the importance which digestion plays in the production of these necrotic lesions, Virchow [1] proposed to call them "corrosive ulcers." Simple and uncomplicated autolysis of the stomach wall is not to be considered.

The causes of the vascular disturbance are another and more obscure matter. They will be discussed separately under the six headings of con-

gestion, embolism, thrombosis, direct vascular injury, vascular diseases and diseases of the nervous system.

I. *Congestion.*—Congestion of the arterioles and venules which is so extreme as to cause rupture followed by hæmorrhage into the tissues is probably the most important single cause of erosions and acute ulcerations of the stomach. The high incidence of such lesions in new-born infants points to the fact that the extreme congestion of all of the abdominal vessels associated with the process of birth is shared by the smaller vessels of the stomach and duodenum and in some of these the pressure is sufficient to cause rupture. In Theile's [2] series of 248 cases of ulcers of the stomach and duodenum in children, 138 occurred in the first year and of these, 83 or one-third of the entire series were found in the first month of life. Butka [3] in 1927 was able to find only three cases of ruptured gastric ulcers in infants under two months of age reported in the literature, although Theile,[2] as early as 1919, was able to collect thirteen such cases. The average age of twelve of these patients was five days, while the thirteenth was seven weeks old. Later in life congestion can be caused by numerous other factors, notably heart disease and cirrhosis of the liver, but ulcerations of the stomach in children with these diseases is not a common or noteworthy finding at autopsy. Talma [4] was able to produce hæmorrhages in the gastric mucosa of rabbits by simple over-distention of the stomach. Following this, there was softening due to digestion with subsequent necrosis and perforation. In an admirable paper by Busch [5] on so-called spontaneous rupture of the stomach, published in 1924, it is pointed out that over-distention or acute dilatation is the commonest predisposing cause in these cases and that the majority have occurred in harvest time due to over-eating of easily fermented fruits and undue consumption of beer. Busch at the same time stresses the fact that other possible causes of rupture, such as carcinoma, chronic ulcers, inflammation of the vessels and thrombosis, must be eliminated before spontaneous rupture of an otherwise normal stomach can be considered. In the patient here reported, thrombosis of the vessels does exist, although there is every reason to believe that over-distention was also present.

II. *Embolism.*—Embolic occlusion of a vessel in any part of the body is possible from any given source. That such lesions in the stomach can occur cannot be denied, or even doubted, although their incidence, judging from the recorded cases, is probably low. Theile [2] collected five cases of ulcers of the stomach in children which appeared to be related to infectious processes in other parts of the body. Two of these were in patients with pneumonia and one each in patients with typhoid fever, measles and scarlet fever. In a series of 165 cases of hæmorrhagic erosions of the stomach which Beneke [6] reported, 66 per cent. were found in non-septic individuals. Schwartz,[7] in 1929, reported three cases in which punched-out or indefinite openings were found in the stomach. The edges of all three of these were exactly as if a hole had been punched out of an area of indefinite inflammatory tissue. In discussing these, he says that it is difficult to speak of an early ulcerative

process and it is better to consider it at a circumscribed necrotic change, the result of rapid and increasing disturbance of nutrition or blood supply to a localized area, the cause most likely being an embolus. No proof for this assumption is given.

Ulceration of the stomach secondary to emboli from an active endocarditis has not been observed in children.

Emboli from the rapidly thrombosing umbilical vein have been considered by Landau [8] to be the cause of the vascular lesions of the stomach and duodenum which have already been mentioned as being frequent in very young infants. He traces these emboli from the venous circulation through a patent ductus botali into the systematic arterial circulation. Such an hypothesis is tenable, although highly speculative.

III. *Thrombosis.*—At the present time, little is understood of thrombosis in any part of the body and a discussion of the various theories of its causes and predisposing factors need not be entered into here. Retrograde thrombosis from other lesions in the peritoneal cavity is perfectly possible and is rather frequently observed following acute suppurative appendicitis. In these cases it need not necessarily be a suppurative process.

Theile [2] devotes considerable space to chronic gastric ulcers occurring in marasmic and weak infants, although no definite exciting cause is mentioned. In four of his collected cases there was perforation of the ulcer. In the 65 cases of duodenal ulcer in Holt's [9] series in which the age was given, 70 per cent. of the ulcers occurred between the ages of six weeks and five months, the greatest incidence being between the sixth and tenth week. Holt says that "the age incidence is very striking. It corresponds very closely with the age incidence of deaths from marasmus." Can not these be due to thrombosis in veins filled with blood which is stagnated as the result of a weakened and inadequate circulation?

Thrombi are present in the vessels of the stomach wall in the case here reported. Whether they are primary or were formed secondary to some underlying and more fundamental process is a matter of opinion only. Definite causes of thrombosis, such as we know them to be, are, in this patient, lacking. We know of no altered chemical reaction of the blood, altered metabolism, slowing of the circulation or injury to the intima of the vessels, although it is futile to deny any or all of these. Such a discussion leads to no end. It is, however, the fact that thrombi were demonstrated in this patient in the vessels in the region of the destructive process in the wall of the stomach which I wish to record.

IV. *Vascular Disease.*—Diseases of the vessel walls can be dismissed without discussion. In adults, changes due to endarteritis and endophlebitis or to hyaline, amyloid and fatty degeneration of the vessel walls might possibly play a rôle in the etiology of ulcerative lesions in the stomach, but in children these changes are of the utmost rarity and the possibility of their occurrence is mentioned only for the sake of completeness.

V. *Direct Injury to the Mucosa.*—Direct injury to the gastric mucosa and underlying blood vessels by caustic and acid solutions, foreign bodies and coarse particles of food must always be kept in mind. These are things which are easier to prove than they are to disprove. In the patient reported, there is a definite history of her having had access to broken pieces of glass three or four days before her death, but at operation and autopsy no foreign bodies could be found, although a careful search for these was made. Chemical analyses of the free fluid in the peritoneal cavity failed to disclose the presence of poisons and there was nothing else in the findings to suggest the ingestion of such substances.

Under the heading of local injuries of the mucosa of the stomach must be noted the tuberculous ulcers which are probably due to the ingestion of tubercle bacilli. Theile [2] collected twenty-one such cases of tuberculous ulcers in the stomach and duodenum of children. One of these in the stomach had progressed to perforation.

VI. *Nervous Influences.*—The neurogenic theory of the origin of vascular occlusion is the one which is included as the final "catch-all" for any case which will not with ease fit into the other groups. It need not detain us long. Spasm in health or disease may occur and this may presumably be limited to certain local areas in the stomach wall. Hauser [10] mentions brain diseases under the causes of hæmorrhagic erosions, but the exact proof of their relation to these changes is not given.

Course.—Hæmorrhagic erosions of the mucosa of the stomach in infants is of rather frequent occurrence and the majority of these progress to healing. Acute ulcerations, on the other hand, are more violent in onset, involve a greater area and depth of tissue and, as a rule, run an acute course, leading in a short time to perforation (Hauser [10]). This tendency to perforation led Rokitansky [11] in 1842 to suggest the name of "perforating stomach ulcers" for these acute lesions. Theile [2] and Hauser [10] both think that in some instances the reparative process may be sufficient to turn these sudden and destructive lesions into ordinary ulcers of the chronic type.

SUMMARY

An acute, fatal, perforated ulceration of the stomach wall is reported in a female infant of twenty-two months of age. The history of ill-health for only two days, the site of the ulcer on the posterior wall near the fundus of the stomach and the lack of all signs of a chronic ulcer lead one to assume that the changes noted are of an acute and rapidly destructive nature. The markedly hæmorrhagic edges of the necrotic area suggest that the primary lesion was one of hæmorrhage, either from local injury, overdistention, or vascular thrombosis, and that gastric digestion of this area caused the perforation. This case is of especial interest in that the perforation was found and measured at operation before post-mortem digestion became manifest.

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ANNULAR PANCREAS, INVOLVED IN ACUTE HÆMORRHAGIC PANCREATITIS

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As far as I have been able to ascertain, the literature has never contained reference to a case at all similar to the one reported in this article.

Case No. G-1526.—The patient, a negro male, aged thirty-five years, a common laborer, entered the Receiving Hospital, January 28, 1929, with an admission diagnosis of (1) chronic nephritis, (2) cardiac hypertrophy, and (3) secondary hypertension. His chief complaint was headache and stomachache. He had felt well until last summer when he began to have pain in his head, throbbing in character, beginning late in the afternoon and lasting the whole night. At about that time, following a sensation of fullness in the head, there was severe nosebleed lasting for ten minutes, leaving him weak. Following this he felt well again until January 24, 1929, when there was noticed slight bleeding from the nose followed by throbbing headaches in the left temporal area, with some shortness of breath and weakness. The shortness of breath had been intermittent since last summer. There had been nocturia for the past three years beginning as two times and now six to eight times. His urine had been light in color and its passage had caused pain and burning for seven months previous to admission and there was also some incontinence since last summer, but no retention. He had been a heavy alcoholic drinker for the past three years until three months ago, consuming one and one-half pints of hard liquor daily. The family and marital histories were unimportant.

Fourteen years ago the patient had a chancre and gonorrhœa. During 1927 he suffered from an attack of parotitis and hæmaturia. In 1928 there was a history of blood-streaked sputum, night sweats lasting for one and one-half years and loss of twenty pounds in weight since June of the same year.

When admitted he was well nourished and well developed. He was apparently not very ill. The teeth showed caries and there was a slight enlargement of the cervical glands. There was limited excursion of the chest wall and diminished elasticity and density of lung tissues. There were no râles or areas of consolidation. A systolic murmur was heard in the third and fourth interspaces with a ringing aortic second sound. The heart boundaries were within normal limits and the blood pressure was 240 millimetres mercury systolic and 170 diastolic. His abdomen in its right upper quadrant showed some tenderness. The liver was not palpable and there was no rigidity nor were there palpable masses or enlarged inguinal glands. The reflexes were normal. The temperature averaged 99° F., pulse 90 per minute and respirations 20 per minute. The specific gravity of the urine was 1.018 to 1.016 with 3 plus to 2 plus albumin and 1 plus white blood cells, no red blood cells, a few hyaline and granular casts at one examination and a few hyaline casts at another. Blood tests gave hæmoglobin 90 per cent. (Sahli), red blood cells 4,250,000 and white blood cells 6,300 to 7,200 with 79 per cent. and 80 per cent. polymorphonuclears. The Kahn and Wassermann tests were negative. The blood nitrogen was 39 milligrams per 100 cubic centimetres and blood urea 32.9 and blood dextrose .11 per cent. The renal concentration test showed the highest specific gravity to be 1.020 with an intake of 1,500 cubic centimetres and an output of 500 cubic centimetres in five hours. A skiagram showed the left ventricle and auricle enlarged. There was practically no hypertrophy of the right auricle.

In February of 1929 there was some improvement, but there was complaint of lack of appetite and considerable abdominal pain, the latter lasting for two days. On February 14, 1929, the patient was discharged.

February 21, 1929, the man was re-admitted to the hospital. The symptoms at this time were those of an acute illness with vomiting of coffee-ground material, rigidity and tenderness of the abdomen, particularly in the right upper quadrant, and severe cramps in the epigastrium and about the umbilicus, protracted through the previous five days and increasing in severity, compelling him to go to bed. The pains were non-radiating in type. The bowels had been constipated for four days but without distention of the abdomen. The patient was in a state of collapse. Palpation revealed an indefinite mass the size and shape of a hen's egg in the right upper quadrant. The temperature at this time was 96.8° and the pulse was rapid. The systolic blood pressure was 130 millimetres mercury and the diastolic 98. The blood nitrogen was 129 milligrams per 100 cubic centimetres, uric acid 12.4 and creatinine 4.

Operation.—It was decided that an acute intra-abdominal surgical condition existed

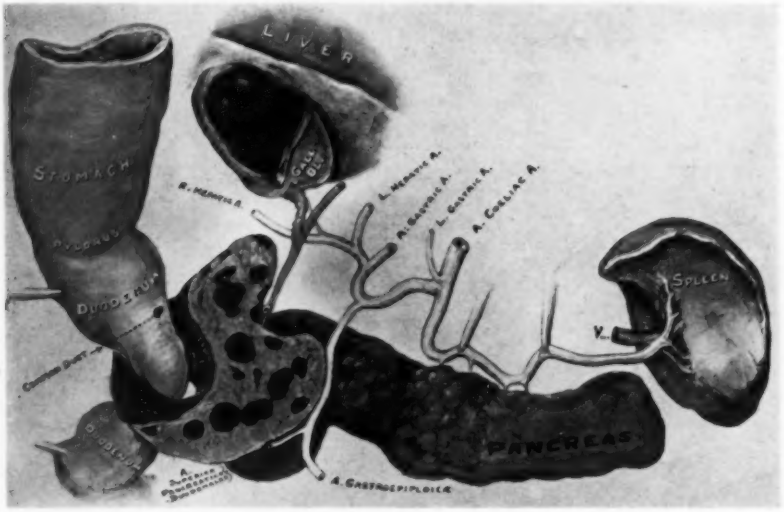

FIG. 1.—Annular head of pancreas.

which was either intestinal obstruction or a walled-off perforated gastric or duodenal ulcer, as there was a definite mass palpable over this area. The abdomen was examined through a four-inch right rectus incision. No free blood was found in the peritoneal cavity but there was extensive sub-peritoneal hæmorrhage involving the cæcum, ascending colon and four feet of the ileum. A massive retroperitoneal hæmorrhage had occurred about the duodenum dissecting beneath the peritoneum as far as and into the pelvis. The hæmorrhage was confined to the right side of the abdomen. The omentum had migrated to the hæmorrhagic area in the right upper quadrant where the retroperitoneal blood had formed a clot measuring about 10 centimetres in diameter. The patient's condition during operation was very poor and stimulants were given. The abdomen was closed with drainage. The patient died one hour and forty minutes later.

Autopsy.—The examination was made twelve hours following death. The cranial cavity showed no pathology. The lungs were essentially negative. The heart was considerably enlarged, the enlargement being due principally to thickening of the left ventricular wall. The valves showed no pathology.

When the abdomen was examined extensive hæmorrhage was found to have occurred beneath the parietal peritoneum on the right side producing bulging into the abdominal cavity. The peritoneum was removed and the hæmorrhage found to be most extensive

about the duodenum. The spleen and body and tail of the pancreas were explored and found to be normal. Blood clot containing considerable fibrin was removed from about the duodenum with difficulty because of the close adherence of the clot. *The head of the pancreas was unusually large and attached to, and apparently growing out from, the anterior aspect of the head and uncinate portion there was a ring-shaped process which completely encircled the proximal end of the descending portion of the duodenum.* (Fig. 1).

Each arm of the annular portion of the pancreas at its attachment to the head measured 2.5 centimetres in its greatest diameter which diminished to 1.5 centimetres at the point most distant from the pancreas proper. The lumen of the annular part measured 2.5 centimetres in diameter, sufficient to allow the duodenum to pass through without constriction. The duodenum proximal to the pancreatic ring, as well as the pyloric ring and stomach, were somewhat distended but this distention was probably recent and due to pressure from the hæmorrhage rather than to a constriction from the annular process. In nearly all reported cases of annular pancreas there was constriction of the duodenum

FIG. 2.—Hæmorrhage, necrosis and leucocytic infiltration.

with consequent dilatation and hypertrophy of the stomach and duodenum proximal to the constriction.

The cystic duct was larger than the hepatic duct, approximating in size the common duct. The cystic, common and pancreatic ducts were somewhat enlarged and were without flexures or angulations. A common bile and pancreatic duct 2 millimetres in length entered the duodenum at the ampulla of Vater. There was but one pancreatic duct which continued without branching for 18 millimetres after entering the pancreas at a point corresponding to an imaginary line of fusion between the pancreas proper and the annular portion. The blood supply of the additional pancreatic tissue was derived principally from the gastroduodenal artery and its superior pancreatico-duodenal branch as well as branches of the inferior pancreatico-duodenal branch of the superior mesenteric. There was an increased number of pancreatic rami of the splenic artery. No accessory branches of the hepatic artery were found.

The enlarged or left side of the pancreatic ring, adjacent to the head, appeared swollen and was somewhat softer than the remainder of the pancreas.

The surface of this portion possessed a red congested appearance and this color spread to the entire surface of the annular pancreas and also to the head and a portion of the body of the horizontal pancreas. Sectioning the organ in the transverse vertical plane, the swollen portion contained numerous areas of hæmorrhage, spherical in shape, measuring from 0.5 centimetre to 1.5 centimetres in diameter. One especially large hæmorrhagic area had ruptured through the capsule, covering the inner aspect of the ring toward the left side of the duodenal wall. This area of rupture communicated with the large mass of blood in the retroperitoneal space. The escaping blood had dissected downward beneath the parietal peritoneum as far as the pelvis and also beneath the visceral peritoneum covering a portion of the bowel, especially the cæcum and ascending colon. The hæmorrhagic areas were confined to the annular portion and the head, except for a single area 7 millimetres in diameter in the tail. Absence of fat necrosis was conspicuous, but it must be remembered that the peritoneum was intact. The gall-bladder was normal in size, but was pale in color and the wall was thickened to ¾ millimetre. There was localized thickening of the gall-bladder wall on the liver side, producing a single, well-circumscribed elevation of 6 millimetres in diameter projecting into the lumen. Here it might be reiterated that the cystic, common and pancreatic ducts were enlarged, straight and continuous, forming an easy pathway for possible infection to travel through the

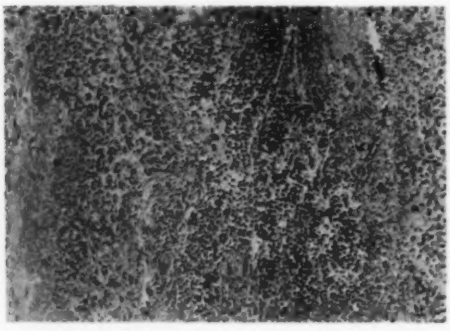

FIG. 3.—An area of suppuration and necrosis.

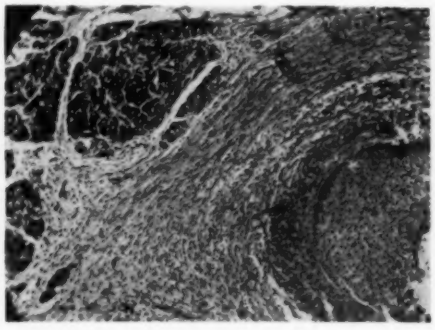

FIG. 4.—Perilobular fibrosis, lymphocytic infiltration and thrombosis. This is a typical area exhibiting chronic inflammation.

ducts from the gall-bladder to the pancreas. The gall-bladder and ducts contained no calculi.

The liver, spleen and entire gastro-intestinal tract were otherwise negative. The prostate was not enlarged. The kidneys were about one-half normal size, pale and fibrous with coarsely granular surfaces. The cut surfaces showed marked connective tissue increase.

The microscopic pathology of the pancreatic tissue can be divided into four interrelated states: 1. An old inflammatory process characterized by marked interlobar and interacinar fibrosis associated with lymphocytic infiltration. 2. Dense pus cell infiltration associated with early necrosis in the central portions of lobules. 3. Larger areas of necrosis involving several lobules with a peripheral zone of purulent exudate. 4. Old and recent hæmorrhage. The recent hæmorrhage was the most extensive, and was associated principally with the large necrotic areas and had probably existed only a few hours before death. The older areas of hæmorrhage were surrounded by a wall of connective tissue, contained hæmosiderin and probably had existed several days.

The gall-bladder wall showed the presence of active chronic cholecystitis.

Discussion.—Differences of opinion exist regarding some minor points in the embryological development of the pancreas. The pancreas develops from cells in that portion of the foregut which later becomes duodenum, differen-

tiating and forming two anlagen in the embryo of 0.75 millimetres in length. The dorsal anlage begins as an outpouching or diverticulum on the duodenum while the ventral anlage arises as a grooved bud from the common duct at its juncture with the duodenum. It is thought that occasionally there are two anterior buds which soon fuse into one. The pancreatic buds are opposite to and appear later than the living buds. These processes grow into the surrounding mesoblastic tissue which forms the capsule and trabeculæ. At first the pancreas is covered by the two layers of mesentery, but as fusion of the mesogastrium and transverse mesocolon occurs, the posterior layer of the mesenteric fold is absorbed, leaving the pancreas behind the peritoneum. In the beginning the hepatic and pancreatic ducts are separate and on opposite sides of the duodenum, but later they approach each other and finally fuse. The anlagen grow separately until by the circumrotation and growth of the ventral anlage around the medial side of the duodenum they meet posteriorly where they coalesce and continue development in one mass in the dorsal mesentery. Up to this time the growth of the dorsal bud is much more rapid than that of the ventral. At first the pancreas is in an antero-posterior position and points upward, but later becomes transverse and horizontal. The dorsal portion of the gland, which is in close proximity to the common duct, corresponds to the ventral enlage which eventually forms the caudal portion of the head of the adult pancreas and the pancreatic duct. The larger portion, derived from the dorsal anlage, represents the remainder of the head and all of the body with enclosed ducts.

If the ventral diverticulum fails to rotate and develops without fusing with the dorsal bud, an accessory pancreas is formed which constitutes the most frequent abnormality of pancreatic development. The accessory pancreas, which is relatively common, is usually found in the wall of the stomach or duodenum and occasionally at the tips of diverticuli of the gastro-intestinal tract, in the formation of which they are supposed to play a part.[1] The accessory pancreas may also be attached to the peritoneal coat of the duodenum and is sometimes spoken of as the "pancreas minus." The "pancreas divisum" results as a separation of gland substance during development due to pressure from the vessels. The semicircular pancreatic process partially surrounding the duodenum is similar to and somewhat more common than the annular pancreas described in this paper. The two distal ends or glandular processes are sometimes connected by a band of fibrous tissue and the circle thereby completed.

Annular pancreas is an extremely rare developmental anomaly. Twenty-eight cases have been previously reported. Ecker[2] gave it the name it now bears in 1862 and is frequently credited with describing the first case at that time. In Smetana's recent article, however, Schirmer (Beiträge zur Geschicte und Anatomie des Pancreas, Inauguration dissertation, Basal, 1893) is quoted to the effect that Becourt demonstrated a case in 1830, and Moyse another in 1852. Auberg[3] reported a similar case four years after Ecker, Symington[4] another in 1885, and Generisch[5] the sixth case in 1890. Since then

cases have been reported or specimens exhibited by Thacher [6] in 1893, Sandras [7] in 1898, Summa [8] in 1900, Tieken [9] in 1901, Vidal [10] in 1905, Lerat (quoted by Huet),[11] Baldwin [12] and two cases by Lecco [13, 14] in 1910, Cords [15] in 1911, Benedetti [16] and also Gruber [17] in 1920, two cases by Kurozawa [18] in 1923, Susukida,[19] Shibata [20] and Keyl [21] in 1924, one case by Sugawra and Shibata [22] in 1925, one case by Thür [23, 24] and three by Smetana [25] in 1929.

To explain the formation of annular pancreas, two theories have been advanced. Due to rotation of the ventral bud, each anlage develops separately, producing pancreatic tissue on each side of the duodenum which might grow, fuse on approximation and eventually surround the gut. The other theory advanced, which is simple hypertrophy, a ventral and dorsal process extending from the head and meeting on the right side of the duodenum with fusion resulting from some "inherent biological force," is more readily understood because, first, there is no marked abnormality of blood supply or arrangement of excretory ducts; second, because the ring is thickest where it joins the head and thinnest on the right side which is most distant from the pancreas proper; and third, the pseudo-annular pancreas may be considered an early or arrested stage of the true annular pancreas, being incomplete because of insufficient hypertrophy.

Lecco [14] believes that the ring portion of the annular pancreas is the left portion of the dorsal pancreatic lobe which has been displaced to the right and he states emphatically that the annular pancreas cannot be explained as a simple, greatly exaggerated proliferation of pancreatic tissue but that its origin is dependent on a dystopic anomaly of the ventral anlage. Cords [15] thinks there is premature fusing of the ventral and dorsal anlage and during rotation of the intestine the ventral part is pulled out into a band. Smetana [25] believes that the theory of the persistence of a left ventral anlage is the most reasonable because it implies only a further development of tissue already present. He also calls attention to the possible development of an increased number of pancreatic buds around the duodenum inasmuch as coëxisting aberrant pancreatic tissue has been found in the gastro-intestinal tract in cases of annular pancreas. Sugawra and Shibata [22] call attention to the observation that annular pancreas is frequently associated with other anomalies in other parts of the body. In Keyl's [21] case there were other developmental defects including a kyphoscoliosis which he thinks might have influenced the shape of the pancreas. Baldwin [12] says "this ring of tissue is either a persistence of the left half of the ventral anlage or an excessive growth from the right half of the same anlage. If it is this latter case the excessive growth has taken place ventral to the duodenum and to the left at the time that the remainder of the same half was growing or being carried dorsally to ultimately fuse with the head of the gland."

Conclusions.—1. The case reported represents the coëxistence of a fairly uncommon inflammatory disease of the pancreas and a rare anatomical deformity of the pancreas which is recognized as a definite entity.

2. The acute inflammation of the pancreas in this case which was asso-

ciated with suppuration, necrosis and hæmorrhage was an exacerbation of an old chronic interstitial pancreatitis, in the presence of chronic cholecystitis.

3. It is possible that annular pancreas is the result of simple hypertrophy rather than an embryological defect, although the rather vague developmental theories are more strongly adhered to.

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SUBACUTE PANCREATITIS OR SO CALLED ACUTE ŒDEMA OF THE PANCREAS*

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The almost hopeless catastrophe of an acute fulminating hæmorrhagic pancreatitis has always seemed to the writer to be a serious reflection upon our surgical progress. Although occasional cases are rescued, even with our improved diagnostic methods and our advanced surgical technic, the mortality still remains appalling. In a collection of 1510 cases from the German clinics, made in 1927 by Schmieden and Sebening, 149 or approximately 10 per cent. of the patients died before operative intervention was possible, and in the advanced cases of necrosis there was an operative mortality of 68 per cent. In the relatively small group which we have had at the Lenox Hill Hospital during the past eight years, our statistics are not much better. From the various services I have found fourteen definite acute hæmorrhagic or necrotic cases. Two died before operation could be performed, the diagnosis being confirmed by autopsy. Three cases survived operation but died subsequently after secondary operations, one of these living as long as fourteen months. Five others succumbed to the operation and four seem to have recovered permanently. The pre-operative mortality was then 14 per cent. plus, the immediate operative mortality was 41 per cent. plus, and the total eventual mortality was 71 per cent. plus. Colp in a recent paper on acute pancreatitis reports slightly better figures. In fifty-one cases of primary acute pancreatitis five died without operation, or 10 per cent. plus, and twenty-three of the forty-six cases operated upon succumbed, or 50 per cent., his total mortality therefore being about 55 per cent.

Apparently out of a clear sky, the patient is stricken by an intensely violent, acute abdominal storm in the most tragic and dramatic manner, and is often moribund before the cause of the disturbance is even suspected, and before there is an opportunity for operative interference. That there has been something radically wrong about our attitude of helplessness on this subject has been my conviction for years. I consider it just as wrong as was our attitude toward the question of diffuse suppurative peritonitis before the whole problem of appendicitis was clarified. I have felt that in many instances this disease must give warning signals long before the terrific abdominal insult occurs, and that if these premonitory symptoms could be recognized, and the disturbance corrected in its early stages, the eventual serious lesion might be avoided. Further, even if the patient is saved from an acute hæmorrhagic disease of the pancreas, this disease with its coincident destruction of the organ, and disturbance in its function, frequently leaves serious sequelæ, notably cysts, nutritional disorders and diabetes. All of

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these might be forestalled if the case is never allowed to reach the acute stage. Still further, if there should be mild previous attacks and even if a serious, acute lesion never occurs, these recurrent attacks of mild pancreatitis must eventually lead to a chronic disease of the organ with fibrosis and all of its attendant disadvantages, which should, of course, be prevented if possible.

I do not propose here to attempt a study of the etiological factors of pancreatitis. I think we are all fairly well agreed that, excluding the comparatively rare traumatic, post-operative and embolic cases, in some way or another a primary disturbance in the biliary system is generally responsible for inflammatory changes in the pancreas. From the clinical standpoint the exact mechanism is relatively immaterial. This may be a reflux of duodenal contents through the duct of Wirsung or the duct of Santorini. It may be a regurgitation through these ducts of either aseptic or bacterially contaminated bile, due possibly to some obstruction at the papilla, perhaps an impacted calculus occluding a pancreatic duct having an anomalous junction with the common bile duct. It may be merely an extension by contiguity, or by a lymphangitis or a phlebitis from an infected gall-bladder, the pancreas being involved in a given case either because of some peculiar virulence or selective action of the causative infective agent, or because of some special anatomical or physiological susceptibility of the organ itself. It is a well-known fact that in the vast majority of cases of pancreatitis, there is an accompanying disease of the gall-bladder, and that usually biliary calculi are found. All surgeons who make a practice of examining the pancreas in cases of gall-bladder disease have had the common experience of finding an enlarged or indurated organ in cases of acute or even chronic cholecystitis. It occasionally happens that, even when there has been a distinct gall-bladder history and where a well-defined gall-bladder lesion is found, the pancreatic condition seems to be the predominating one, and the gall-bladder disturbance of secondary importance, as the following rather striking example illustrates:

Case I.—A. H., female, age thirty-eight years, was admitted to the Lenox Hill Hospital to the service of Dr. Otto Hensel October 18, 1926. She gave a typical history of recurrent biliary colic of five years' duration. For two weeks she had been acutely ill, suffering from pain in the right upper quadrant radiating to the back, nausea and vomiting. There was marked tenderness and rigidity in the right hypochondrium, and also some sensitiveness in the left hypochondrium. She was distinctly jaundiced. The temperature on admission was 100.4°, the pulse 80. The blood count was normal. The urine showed a trace of albumen, no sugar, and considerable bile. The icterus index was 41.0. The van den Bergh reaction was, direct, positive both immediate and delayed; indirect, positive. The blood sugar was 102 milligrams and the blood cholesterol 125 milligrams per 100 cubic centimetres of serum. X-ray examination showed a poorly functioning gall-bladder with shadows strongly suggesting calculi. The afternoon temperatures ranged from 100° to 102.6°, and she was finally turned over to the surgical service and was operated upon by Dr. Otto C. Pickhardt October 30, 1926, with a provisional diagnosis of subacute cholecystitis and cholelithiasis. A somewhat enlarged gall-bladder with rather thickened walls was found. The gall-bladder contained several medium-sized mulberry calculi. There was an induration around the cystic duct, but there were no calculi in the cystic or common bile ducts. What was particu-

larly striking was that the pancreas was about twice its normal size and very much indurated, especially at the tail. The patient made an uneventful convalescence after cholecystectomy and has remained well since. The gross examination of the gall-bladder did not suggest an acute lesion, the microscopic report was chronic cholecystitis, and a culture from the bile was sterile.

Here was a case of very obvious gall-bladder disease with rather acute symptoms, but with the pathological findings in the gall-bladder not corresponding in acuteness to the clinical picture. On the other hand, the pancreatic condition was very pronounced, and was apparently the more important factor in the patient's illness. This characteristic but not uncommon combination could readily be multiplied by other similar ones from our hospital records and my personal experience, but I believe it suffices to show that there is found, occasionally, even with a frank gall-bladder pathology, a still more marked lesion of the pancreas. This lesion is usually of the subacute variety and is rather conclusive empiric evidence that a disturbance in the biliary system, generally some form of cholelithiasis or cholecystitis, is the usual causative agent in pancreatitis.

For some obscure reason, until very recently, only two varieties of pancreatitis have received any real recognition from the pathologist and the clinician—the acute hæmorrhagic or necrotic, and the chronic types. Why is it not fair to assume that milder, preliminary attacks occur before an acute serious lesion or a chronic fibrosis has developed? Cannot these milder attacks be recognized and treated, and cannot, by treatment, the danger of further trouble be avoided?

There is surprisingly little reference to the subject in the literature. Not until 1922 did Zoepffel first suggest this possibility. This author called the condition an acute pancreas œdema, which, he believed, was a premonitory stage of an acute pancreas necrosis. He reported on four cases in which he had done a cholecystectomy with T-drainage of the common bile duct, and tamponade of the exposed pancreas. He found in all these cases, in addition to a more or less acutely inflamed gall-bladder containing calculi, a swollen, œdematous pancreas without hæmorrhage or necrosis, but in two there were fat necroses. In two cases probatory excision of pancreatic tissue showed inflammatory œdema without necrosis of the parenchyma and without hæmorrhage. All four cases made uneventful recoveries.

Apparently the subject aroused no further interest until 1925 when Katsch reported on six clinically observed cases of mild pancreatitis, unconfirmed by operation or autopsy. He emphasized particularly the importance of deep epigastric pain radiating to the left hypochondrium as a diagnostic symptom. All of his cases recovered. In 1927 Schmieden and Sebening, in a most comprehensive paper on the surgery of the pancreas, read before the Deutsche Gesellschaft für Chirurgie, referred to Katsch's paper very casually, and left a further consideration of the matter to G. von Bergmann, who discussed their paper from the standpoint of the internist.

To clarify the question and to confirm the impression that such a form of mild pancreatitis could occur and give a distinct, independent pathological

and clinical picture, it was necessary to find a case, verified by operation, which was practically free from gross gall-bladder pathology, and where the pancreatic involvement was the essential factor. Such a situation had not yet been reported. It was my good fortune, recently, to have encountered the following typical instance:

CASE II.—N. K., male, age forty-six years, consulted me June 1, 1929. Without any history of previous attacks, he awoke the morning before with severe, diffuse abdominal pain, referred particularly to the epigastrium. He was nauseated and induced vomiting and could obtain relief only by a hypodermic injection of morphine. The pain continued to recur and was very definitely concentrated in the epigastrium, radiating to the back and especially to the left. It was very intense and required a second dose of morphine. Otherwise the patient was not very acutely ill. On examination there was some sensitiveness on deep pressure in the epigastrium, but no particular rigidity. There was no jaundice. The temperature was 100.8° and the pulse 80. The next morning he was somewhat improved, but that evening there was again very severe pain. June 3, 1929, he was admitted to the Lenox Hill Hospital. He had a normal blood count. The urine showed no albumen or sugar. His temperature was 99.6° and his pulse 90. The X-ray examination of the stomach and duodenum was negative. Owing to the patient's condition, the taking of a gall-bladder series was regarded as impracticable. June 5 the pain again became very intense so that the patient required five doses of morphine during the day. It was of a severe, boring character, referred largely to the mid-epigastrium, with some radiation to the left. His temperature rose to 101.6°. Operation was decided upon. A tentative pre-operative diagnosis of acute cholecystitis or possibly subacute pancreatitis was made. The operation was performed June 6, 1929. The following findings were noted: There was no free fluid in the peritoneal cavity. The gall-bladder was slightly thickened but not injected or distended. No calculi were found in the gall-bladder, ducts or at the papilla. There were no adhesions to the gall-bladder. There was some slight fibrosis of the capsule of the liver at the edge of the right lobe, but otherwise there was no gross pathology of the liver, stomach, pylorus, or duodenum, or of either kidney or the spleen. The foramen of Winslow was patent. There was a distinct and marked swelling of the pancreas which was about half again its normal size, and the entire organ was definitely indurated. The overlying peritoneum from the posterior wall of the lesser sac was intensely injected and œdematous, but there was no evidence of suppuration, hæmorrhage or necrosis in the pancreas, nor were there any fat necroses. Although the gall-bladder was slightly thickened, the lesion in the pancreas was the outstanding pathology. Cholecystectomy was performed. Then through an opening in the gastrohepatic omentum, the peritoneum covering the pancreas was widely split transversely and two cigarette drains were led down to the organ. Two cigarette drains were also inserted past the cystic duct stump to Morison's pouch. The gall-bladder was somewhat thickened and contained thin, dark, amber-colored bile, a culture from which showed no growth. There were no calculi in the gall-bladder. Microscopic examination showed a chronic cholecystitis. The patient's convalescence was rather stormy. He first had an almost complete suppression of urine, lasting for three days, and subsequently developed a post-operative psychosis, possibly of uræmic origin. His severe, deep epigastric pain ceased, however, almost immediately after the operation, and eventually he made a complete and satisfactory recovery, with primary union of the sutured portion of the wound. For a time there was a mucopurulent discharge from the pancreatic drainage sinus, but this eventually closed. He has been perfectly well since. This was clearly a very early and relatively mild pancreatitis of the subacute type, which was almost diagnosed, associated with a comparatively insignificant chronic cholecystitis without calculi.

After my experience, another almost identical case was observed at the Lenox Hill Hospital by Dr. Otto C. Pickhardt.

Case III.—S. G., male, age thirty-nine years, was admitted to Doctor Pickhardt's service October 14, 1929. He had been in the hospital twenty-two months before, complaining of a severe pain in the upper abdomen radiating to the back from which he had been suffering on and off for the past three years. He had never been jaundiced. He had not been acutely ill and never had had any rise of temperature. Various examinations suggested the possibility of a duodenal ulcer. He was discharged after a two months' period of observation without any surgical interference. On his re-admission, he gave a history of having been quite well until four months previously, when he began to complain of a sensation of pressure in the right upper quadrant. This was followed by a deep, dull pain in the mid-epigastrium and back, radiating to the right side. Two weeks before admission, the pain became knife-like in character and of great severity. The patient stated that although he was twice shot in the abdomen during the war, he had never experienced such pain as he suffered from during the present attack. The pain then began to radiate to the right shoulder. He required large doses of sedatives. There was no nausea or vomiting. Examination showed a well-nourished individual. He was not jaundiced. There was tenderness on deep pressure in the epigastrium, but no rigidity. His pulse and temperature were normal. His blood count was normal. The urine showed no albumen or sugar. The icterus index was 4 to 5. He was operated on by Doctor Pickhardt October 16, 1929, with a pre-operative diagnosis of duodenal ulcer or possibly subacute cholecystitis. A relatively normal gall-bladder was found, except that there were a few pericholecystic adhesions. There were no calculi in the gall-bladder, ducts, or at the papilla. The foramen of Winslow was open. The head of the pancreas was found to be enlarged to the size of a plum, indurated and nodular, and the body and tail were much firmer than usual, but not so indurated as the head. There were several enlarged, hard lymph glands lying over the head of the pancreas and one of these was removed for microscopic examination. The gall-bladder did not seem sufficiently diseased to warrant cholecystectomy, but through the gastrocolic omentum, the peritoneum over the head of the pancreas was incised. This tissue was found to be much thickened, œdematous and bled profusely on incision. The area was drained by two cigarette drains. Microscopic examination of the excised lymph gland showed a chronic lymphadenitis with surrounding inflamed fat tissue. The patient made an exceptionally uneventful convalescence except that for a time he still complained of deep epigastric pain similar in character to that from which he had suffered before the operation. Up to twelve days after the operation, the urine contained sugar up to 0.7 per cent. For a time there was a mucopurulent discharge from the drainage sinus which, however, showed no active pancreatic ferments. Doctor Pickhardt reports that he has recently seen the patient, who has remained perfectly well since his discharge from the hospital. This case was also a clearly defined subacute affection of the pancreas, without definite gross involvement of the gall-bladder.

Following these cases, a paper by Archibald, of Montreal, appeared in the November, 1929, Annals of Surgery entitled "Acute Œdema of the Pancreas". His paper is based on some animal experimentation, and an observation, similar to the last two cases reported above, which he made during an operation in 1907. He is also of the opinion that there is a form of mild pancreatitis which may be a precursory stage of the much more serious acute hæmorrhagic or necrotic form, or of the chronic type of the disease, which might possibly be recognized, and which may be amenable to surgical treatment. He advocates cholecystostomy as the operation of choice.

How then can these various ideas and experiences be correlated into a

definite pathological and clinical picture? What are the pathological criteria by which subacute pancreatitis or so-called acute œdema of the pancreas may be established as a distinct entity? If it exists, what is its symptomatology, and how can it be differentiated from the acute or chronic form, and from other subacute conditions in the upper abdomen? Finally, if it can be diagnosed, how should it be treated?

Pathologically, in order to be grouped in this category, the pancreas should show only an enlargement and induration, largely due to œdema. If there is true suppuration, frank hæmorrhage, or actual necrosis, with the usual escape of pancreatic ferments and the formation of fat necroses, the case must be classed as belonging to the acute variety. In addition to the increase in size and thickening of the pancreas, the overlying peritoneum from the posterior wall of the lesser sac will be found to be œdematous and injected. Further, in order that the case may be considered clean cut, there should be no, or only very slight, gross disease of the gall-bladder. In the chronic form there is, of course, also an enlarged pancreas, but it is firmer and more fibrous, and there is no œdema or injection of the overlying peritoneum. The microscopic examination according to Zoepffel, as mentioned above, shows only inflammatory œdema of the gland without any necrosis of the parenchyma and without hæmorrhage.

From the clinical aspect, unless the case is obscured by a complicating active disturbance in the gall-bladder or bile ducts, the picture is rather characteristic. There is usually a definite history of previous recurrent attacks of pain, extending over a period of a few months to many years. In a study of the acute hæmorrhagic cases, it will be seen that with very few exceptions, there is such a history. In our small group, this history was obtained in twelve out of the fourteen cases, or 85 per cent. plus. In one of the cases no reference is made to previous attacks, and in one it is stated that the acute disturbance was the first attack. These attacks vary in severity and duration and, of course, subside spontaneously until the serious acute involvement occurs, or until a chronic pancreatitis is established. It might be argued that these previous attacks were attacks of biliary colic or cholecystitis. This is probably correct in certain cases, but in many instances, if the attacks are analyzed, they will be found to have a rather specific character, differing decidedly from the usual gall-bladder pain. Further, it will be seen that in some of the cases where there have been previous severe attacks, the gall-bladder is found relatively uninvolved—at least grossly. This was true in two out of our fourteen acute cases, and also in the subacute Case III reported above.

The pathognomonic symptom is an excruciating, deep, boring pain in the mid-epigastrium. In the last two cases reported here, this pain was of the severest character—and this feature has been confirmed by all the other observers. The pain usually radiates to the left, as emphasized by Katsch and as noted in Case II. This fact helps to differentiate the disease from a gall-bladder condition, or from a penetrating duodenal ulcer, but it is by

no means inevitable. In Case I, the main pain was in the right hypochrondrium, and this radiated to the back, due probably to the definite gall-bladder pathology. In Case III, the pain radiated to the right, probably because the principal involvement was in the head of the pancreas. Nausea and vomiting may accompany the pain but they are not outstanding symptoms.

The main objective sign is tenderness on deep pressure in the epigastrium with practically no, or only very slight, rigidity. The absence of real peritonism is obviously due to the fact that the inflammatory condition lies so deep in the abdomen that a *defense musculaire* is precluded. There is often a definite Head zone of hyperæsthesia in the left flank at the level of the eighth to the tenth dorsal. Except when there is a calculous or inflammatory common bile duct obstruction, due to a complicating cholelithiasis or choledochtitis, jaundice is usually absent and there is generally no increase in the icterus index figures. There is frequently a moderate rise of temperature and a slight elevation of the pulse rate, but this is not excessive, so that aside from the extreme pain, the patients do not appear acutely ill and the entire picture of the disease is definitely that of a subacute disturbance. There may be some leucocytosis, a trace of glycosuria, or a mild degree of hyperglycæmia. A decreased sugar tolerance may also be noted. An increase in the amylase or lipase content of the blood or urine may likewise occur. Finally, there may be a diminution or absence of the pancreatic ferments in the duodenal contents obtained by the duodenal tube.

This clinical picture should serve sufficiently to differentiate this disease from the two conditions with which it might most readily be confused, namely, a mildly acute or a subacute cholecystitis, and a penetrating gastric or duodenal ulcer. A negative X-ray examination of the gall-bladder, stomach and duodenum, which would be found in an uncomplicated subacute pancreatitis, should help to settle the diagnosis.

Assuming then that this type of pancreatitis occurs, and that it can be diagnosed, what is the proper therapy? I believe that early operative interference is distinctly indicated, both as a curative and as a prophylactic measure, even if the possibility of a subsidence of a particular attack exists. Contrary to the opinion rather generally held, I believe that, if a definite subacute pancreatic involvement is found, a cholecystectomy should be done in the majority of cases, even if there is no very decided gross lesion of the gall-bladder. I feel that the removal of the gall-bladder removes the main source of danger. The cystic duct stump area should certainly be drained in these cases, as leakage from explosion of the ligature is not improbable, but I do not believe drainage of the common bile duct is usually necessary. The only exception I would make to this indication is if the patient is jaundiced, which would point to a more chronic form of the pancreatic disease, and some obstruction at the papilla of Vater. In such a case the gall-bladder should be preserved and a cholecystostomy done with the intention of performing an eventual cholecystectomy when the jaundice has subsided and the biliary fistula has closed. A cholecystenterostomy or a cholecysto-

gastrostomy should be reserved for the frankly chronic cases with definite and more permanent occlusion at the papilla. On the whole, if the gall-bladder is not needed as a safety-valve, I think it is better to remove it because of the numerous disadvantages that follow in the wake of a retained, cholecystostomized gall-bladder which have been pointed out by many authors, and to which I have also called attention. In general, I believe that the possibility of the development of pancreatitis is just an additional point in favor of the removal of a diseased gall-bladder. Of course should calculi be found in the common bile duct or at the papilla, these should be removed with or without drainage of the duct, depending upon the presence or absence of a coëxisting cholangitis.

Though somewhat of a negative argument, it is an interesting observation and rather confirmatory as to the etiology and prophylaxis of acute hæmorrhagic pancreatitis that, although an acute pancreatitis may develop after removal of the gall-bladder as a post-operative complication, due to trauma, or to an extension of an acute gall-bladder infection, I have been unable to find a single case in my own personal files, our hospital records, or the literature as a late sequel to cholecystectomy. It is true that occasionally, after cholecystectomy, the patient suffers from attacks of epigastric pain which suggest pancreatitis, but these attacks are usually of a mild character and generally subside spontaneously. I have had one experience after cholecystectomy where re-operation became necessary because of severe epigastric pain, vomiting, slight jaundice, and a rise of temperature to 101°. Extensive adhesions were found, producing a definite kinking and a dilatation of the common bile duct, with marked induration of the entire pancreas, particularly of the head. Separation of the adhesions and straightening out of the common bile duct led to an uneventful recovery.

In addition to the cholecystectomy, I believe that the pancreas should be exposed, preferably through the gastrohepatic omentum. If this is too shrunken to give easy access, an opening in the gastrocolic omentum may be made. The peritoneum overlying the pancreas which constitutes the posterior wall of the lesser sac should be transversely incised as widely as possible, but care should be taken not to enter the substance of the gland itself. This form of decapsulation relieves the congestion and œdema and helps to restore the gland to its normal condition. Cigarette drains should be led down to this area.

My associate, Dr. Walter T. Stenson, and I have made a series of anatomical studies on the cadaver to determine, first, which is the most satisfactory approach to the pancreas, and, second, whether the pancreas has a capsule of its own in addition to the overlying peritoneum. We have found that the pancreas is by far most easily accessible through the gastrohepatic omentum, from an opening in which it can be readily exposed for its entire length. We have found further that the pancreas has no real capsule of its own, either macroscopically or microscopically. It simply lies retroperitoneally and is covered by the peritoneum, which comprises the posterior wall of the lesser sac and which is delicately adherent to the gland.

As to prognosis, the immediate operative results, barring unexpected complications, should be most satisfactory. The patients are not violently ill and the risk seems to be minimal. There appears to have been no direct mortality after operation on a straightforward case of subacute pancreatitis. The end-results also seem to be good, although the problem is too recent, the number of cases reported is still too small, and the period of observation is too short for definite conclusions to be drawn. While the possibility of a recurrence of the pancreatic disturbance after cholecystectomy and decapsulation cannot be denied, serious trouble seems unlikely. In the three cases reported above, the first patient has had no recurrence of attacks for three years and five months, and the second has been well for ten months. In the third case, cholecystectomy was not done so that no conclusion can be drawn regarding the effect of this procedure, but following only the splitting of the peritoneum over the head of the pancreas, the patient has been free from symptoms for nearly six months.

Summarizing these observations, I feel that there is sufficient evidence to warrant the belief that a subacute or mild pancreatitis, or so-called acute œdema of the pancreas, does exist as a pathological and clinical entity, independent of frank, outspoken gall-bladder disease, though it is most likely due to some primary disturbance in the biliary system. In all probability it occurs much more commonly than has hitherto been supposed. It also seems probable that this condition is a forerunner of the acute hæmorrhagic or necrotic, and possibly also of the chronic varieties. Further, the clinical picture of this form of pancreatitis is sufficiently typical for a diagnosis to be made in the majority of instances. Finally, early operative interference, usually cholecystectomy, combined with splitting of the peritoneum overlying the pancreas, and drainage of the surface of the gland, the approach being preferably through the gastrohepatic omentum, appears to be indicated, and offers a favorable immediate and ultimate prognosis.

In conclusion, I wish to acknowlege my indebtedness to all my colleagues at the Lenox Hill Hospital who have so kindly placed their clinical material at my disposal.

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DISCUSSION.—DR. OTTO C. PICKHARDT said that, as several of his cases had been mentioned by Doctor Stetten, he felt in a position to discuss several points that were of interest to him. First, the diagnosis: This is difficult and not so simple as Doctor Stetten makes it seem. As to symptoms, if the subjective ones were tabulated, half would fit under the gall-bladder and half under the duodenal ulcer caption. Specifically, the food symptoms were those of ulcer, the pain symptoms those of the gall-bladder, both in severity and type. The objective symptoms were such that they also could be caused by either a cholecystitis or an ulcer lesion. In one of the cases mentioned, the X-rays were curiously unreliable. On one examination a diagnosis of duodenal ulcer was made with the gall-bladder plates normal, while on succeeding examinations a diseased gall-bladder was diagnosed with a normal duodenum; whereas at operation, both the duodenum and the gall-bladder were found to be normal. Here, then, is a condition of which Doctor Pickhardt, for one, could not make a sure pre-operative diagnosis, but had to advise an exploration. Possibly the findings of an occasional fleeting glycosuria might be of value here. Doctor Stetten had expressed regret that in this case the gall-bladder was not removed. Now that organ was as normal as any that could be seen—thin-walled, greenish, translucent and showing absolutely no signs of inflammation. That brings up the question of the etiology of the pancreatitis; in this case it was evidently not biliary, but possibly due to an infection backward through the excretory duct of the pancreas, through the duct of Wirsung or of Santorini by the entry or reflux of intestinal juices. Anatomically, this is easily possible, as a separate opening into the duodenum or the common duct is not unusual. Certainly, the removal of a normal gall-bladder would not remedy that state of affairs. If one admits the possibility of an acute pancreatitis from causes outside the biliary system, it necessarily follows that the gall-bladder may be perfectly normal and hence its removal is not indicated. When the gall-bladder is diseased, of course, it should be removed, but should more be done? Should the pancreatic covering be incised and drained? Doctor Pickhardt thought it should. And still, when one remembers, one thinks of cases done by oneself and associates where the gall-bladder did not seem nearly acutely diseased enough to account for the symptoms and yet, after removal, the patient was apparently cured. Here, probably, the pancreas was involved, but that fact did not stand out sufficiently. Hence, a more thorough examination of the pancreas should be made in all these cases. The speaker said he believed that Doctor Stetten has made a valuable contribution to pancreatic literature.

DR. FREDERIC W. BANCROFT asked Doctor Stetten how obvious it is at operation that the pancreas is diseased. He recently saw a case with extreme epigastric pain which was diagnosed before operation as penetrating ulcer. At operation, nothing was found to account for the patient's pain. The man was a painter, but there was no evidence of lead poisoning, and a thorough study of the nervous system and blood-tests appeared to exclude

syphilis. Since hearing this paper, it occurred to the speaker that this might have been a case of subacute pancreatitis.

Dr. Ralph Colp said that he was glad to learn that the difficulty of the diagnosis of acute pancreatitis existed not alone at Mount Sinai Hospital but at other hospitals as well. He recently had had a patient who had suffered previous attacks with symptoms which sounded like those of gall-bladder disease, and at operation the gall-bladder appeared normal. It was barely possible here that the pathology may have been due to œdema of the pancreas. In some cases of acute pancreatitis glycosuria has been noted, but this finding would not be important in œdema of the pancreas since it is unaccompanied by pancreatic destruction. Doctor Colp took exception to Doctor Stetten's rationale of treatment. If the gall-bladder appears normal there is little chance of œdema of the pancreas being due to the extension of the infection along the lymphatics to the pancreas. It is more than likely that most cases of acute pancreatitis and possibly œdema of the pancreas are due to a retrojection of bile up the pancreatic duct, dependent on anatomical varieties. If this is so, then external drainage of bile is indicated. In a group of forty-three cases where the gall-bladder was examined, forty-one showed definite pathology of the gall-bladder, and in two, the gall-bladder was reported normal and was drained; stones subsequently extruded through the cholecystostomy wound. The initial attack may have been due to impacted stones.

Therefore, the speaker could not see whereby the removal of the gall-bladder alone would help the pancreatitis unless this was accompanied by common duct drainage. It is difficult to drain the choledochus with a T tube, but it would not be difficult to drain the common duct via the open cystic duct, placing the drainage down to it.

Dr. Carl Eggers said that Doctor Stetten had alluded to the duct method of invasion of the pancreas and it is probably that method which leads to the acute cases of pancreatitis. There is no certainty as to the etiology of pancreatitis. One group of writers favors the theory that an influx of bile or duodenal contents through the duct starts the process, while another group believes that pancreatitis is an infection due to lymphatic invasion from without, usually from the biliary system. Mann and Giordano, of the Mayo Clinic, have shown that reflux of bile into the duodenal duct is possible in only a small percentage of cases. It has seemed to Doctor Eggers, on the basis of personally observed cases, that it is this small group of cases, in whom the anatomical conditions are favorable, that pancreatitis occurs. Certain it is that in acute pancreatitis one nearly always finds associated gall-bladder disease. This gall-bladder disease is not acute, but either chronic cholecystitis or cholelithiasis and there is no evidence that infection as such plays a rôle. In his own cases he had taken cultures of the peritoneal and the retroperitoneal fluid, as well as of the gall-bladder, and he found no positive cultures. He believes that the entire condition is chemical rather than infectious in character. In case spread of infection from the gall-bladder

played a rôle, one would have clinical symptoms referable to the gall-bladder for some time previous to the onset of pancreatitis, but that is not the case. The patients are stricken suddenly and are at once critically ill. Something has happened, probably an influx of bile. Several of Doctor Eggers' patients had repeated attacks, one as many as eight attacks, but it is impossible to say whether they were due to gall-stones or to milder forms of pancreatitis than the attack for which operation was performed.

For the type of pancreatitis reported by Doctor Stetten, and which he calls subacute, it may be possible to assume lymphatic invasion from without as the etiological factor. It is difficult to say of how much clinical importance this condition is, and whether it can be diagnosed. If one believes that there is a close relation between gall-bladder disease and pancreatitis the treatment advanced by him, namely cholecystectomy and drainage through the cystic duct, seems a rational one. The speaker stated that in his own experience the milder forms of pancreatitis were rare. He had made it a practice in most of his gall-bladder cases to palpate the pancreas and it had usually been found in a condition which he considered normal. Even if it seemed a little larger or harder the condition was difficult to interpret, as there was no definite change. At any rate, as long as the operation was undertaken for the cure of cholecystitis or cholelithiasis, and the gall-bladder was removed, the pancreatic condition would spontaneously clear up. He had seen no case of pancreatitis develop after cholecystectomy.

Dr. Alexis V. Moschcowitz regretted, in a measure, the new subdivision proposed by Doctor Stetten because, from long experience, he has found the entire question of pancreatitis sufficiently difficult and only after many years of study did his views finally become crystallized. In short, he divided these inflammatory diseases of the pancreas into two main groups: namely, acute and chronic. The first group is very frequently undiagnosticated and is characterized by more or less extensive areas of fat necrosis, and frequently also by hæmorrhage in and about the pancreas. Some of the cases go on to the development of cysts, abscesses and even gangrene. The second group, *i.e.*, cases of chronic pancreatitis, are usually diagnosticated in the course of operations for presumed cholecystitis, and are characterized by very firm induration in the head of the pancreas. As to the treatment, Doctor Moschcowitz was not quite certain. He is by no means convinced that the much-lauded operation of cholecystostomy is *sine qua non*. He well remembers operating on two cases of acute pancreatitis in which all that was done was an exploration of the abdomen, in order to establish the diagnosis, and an incidental appendectomy, and yet both patients made an uninterrupted recovery. On the other hand, he also remembers a case which he reported on a previous occasion. The patient was exceedingly ill and was operated on for supposed cholecystitis. There were no gall-stones, but an acute pancreatitis with hæmorrhage was found. Cholecystostomy was followed by complete recovery and the patient was ready to be discharged from the hospital with directions to continue the drainage for at least three months. On the night

before her discharge from the hospital, with a perfectly functioning cholecystostomy, the patient was again seized with violent symptoms and at re-operation an enormous, fresh, peri-pancreatic hæmorrhage was found, from which the patient succumbed. Doctor Moschcowitz did not wish to deny the existence of the symptom complex as described by Doctor Stetten, but was inclined to the belief that it is exceedingly rare.

Dr. Joshua F. Sweet called attention to the necessity of clearly distinguishing between the condition of acute pancreatitis and the condition of chronic pancreatitis. Acute pancreatitis seems to be caused by the activation of trypsinogin into trypsin, not where it normally occurs—in the lumen of the intestines—but within the tissues of the pancreas itself. This proteolytic ferment digests everything with which it comes into contact, including blood-vessel walls—therefore the hæmorrhage.

Chronic pancreatitis, in Doctor Sweet's opinion, is a lymphangitis, progressing from the lymphangitis of the bile passages. The reason for this belief is that the condition is often limited to the "triangle of pancreatic involvement," that is, to that portion of the pancreas which is derived from the persisting ventral anlage. This portion of the pancreas develops from one of two buds which grow out from the primitive intestine very close to the liver bud, or even from the lower part of the liver bud. The lymphatics of this part of the pancreas are, therefore, in very close relation with the lymphatics of the bile-ducts.

This concept of an acute œdema of the pancreas has never been clear in the matter of the origin of the excess fluid. An excess of fluid in tissue occurs as a concomitant of inflammation, and is then associated with extravasation of white and red cells; a simple œdema results from back pressure in the lymphatics.

Does Doctor Stetten conceive of this condition as an early stage of the acute disease?

Dr. Morris K. Smith said that in view of the theory of reflux of bile as a cause of pancreatitis he wished to cite a personal experience. He operated on a young woman for acute pancreatitis and drained the gall-bladder after removing some stones. The patient convalesced satisfactorily until such time as the biliary drainage had ceased, or practically so, when suddenly there developed severe pain deep in the epigastrium and back accompanied by elevation of temperature, rapid pulse and all the appearance of an attack similar to that with which she entered hospital. The sinus tract was probed with a re-establishment of biliary drainage and prompt subsidence of symptoms.

Dr. Seward Erdman said that from the observations he had made at the New York Hospital in these cases, he endorsed Doctor Stetten's statements as to the clinical entity. To the speaker's knowledge, only about three cases have been correctly diagnosed before operation, on the Second Surgical Division of the New York Hospital during the last fifteen years, as acute pancreatitis. The diagnosis of acute pancreatitis is difficult. In view of Doctor Sweet's

paper read before this Society last May, in which he claimed that no bile ever leaves the gall-bladder by the ducts, how can Doctor Sweet now state that infected bile from the gall-bladder goes to the pancreas? By a rather odd coincidence, on the day the programs announcing the subject of that evening's paper were received, a patient was admitted to the hospital presenting the essential features of this diagnosis. The patient referred to came in as an acute appendicitis; there was no rise of temperature nor increased rapidity of the pulse, but there was great abdominal pain at the onset. There was no history of previous attacks. He held himself very rigid. The one notable observation was the presence of a prominent ridge across the epigastrium which led to the inclusion of this case among the three cases of pre-operative diagnosis of pancreatitis. At operation by Doctor Garlock, the only finding was a definitely enlarged pancreas. The gall-bladder was palpated and found normal. A drain was put down to the pancreas and nothing was done to the gall-bladder; if anything had been done it would have been a cholecystostomy, for the patient was very sick and in great pain. He made a perfectly smooth convalescence. Doctor Erdman asked Doctor Stetten why he believes there is special virtue in incising the posterior peritoneum, covering the pancreas. Such incision of the peritoneum, which merely covers one aspect of the organ, cannot act to relieve tension in the pancreas.

Dr. Henry H. M. Lyle referred to a case of acute pancreatitis which he had shown before this Society fifteen years ago in which nothing was done to the gall-bladder but a portion of the head of the pancreas, being gangrenous, was removed. After a stormy convalescence the patient got well.

Dr. John Douglas said that as Doctor Eggers had stated, there are cases in which there are recurrent attacks of pain in which it is impossible to say whether the gall-bladder or the pancreas is involved. Several years ago Doctor Douglas had a patient with acute pancreatic necrosis, on whom he operated and found a large number of stones in the gall-bladder. The patient died. At autopsy a large, necrosed hæmorrhagic condition was found in the head of the pancreas. Further back there were areas where the pancreatic tissue was replaced by thick, creamy material, the result of breaking down of pancreatic tissue in previous attacks. It seemed to Doctor Douglas that the terminology "itis" indicates an inflammatory condition. Whether acute involvement of the pancreas is due to reflex of bile, or a reflex of intestinal contents into the pancreatic duct, or whether it is due to the activation of pancreatic ferments, as suggested by Doctor Sweet, it is not an inflammatory condition and it would seem, therefore, that pancreatic necrosis was by far the better term to give a right impression of the lesion present in this acute condition of the pancreas.

Doctor Stetten, in closing the discussion, replied to Doctor Bancroft's question, "How obvious is the pancreatic lesion?" that in the case he had observed it was a very typical and definite condition. The gall-bladder was

not involved grossly, but the pancreas, examined through the gastro-hepatic omentum, was found to be half again its normal size and of very firm consistency. The overlying peritoneum of the posterior wall of the lesser sac was intensely injected and œdematous, but there was no hæmorrhage, necrosis or suppuration. In answer to Doctor Colp, regarding the indication for cholecystectomy, Doctor Stetten said that he believes Doctor Colp's own statistics justify this procedure. Doctor Colp stated that in forty-three cases in which the condition of the gall-bladder had been noted, this organ was found obviously diseased in forty-one instances. Without entering too deeply into the question of etiology, Doctor Stetten thinks that these figures rather strengthen the theory that disease of the gall-bladder is usually in some way or another connected with the pancreatic involvement, and on this basis, he feels that it is safer to perform a cholecystectomy. Answering Doctor Sweet, Doctor Stetten said that he believes that the lesion is really an inflammatory condition, irrespective of whether the cause is bacterial or chemical, and that the œdema is a precursor of the more destructive lesion. Referring to Doctor Erdman's question, Doctor Stetten stated that he believes that the cystic duct region should always be drained after cholecystectomy in these cases. He also believes that, although the pancreas has no definite capsule, the overlying peritoneum of the posterior wall of the lesser sac acts as a pseudo-capsule, which Doctor Stenson and he found to be delicately adherent to the pancreas. He feels that the splitting of this peritoneum acts as a form of decapsulation, which reduces the congestion of the organ, facilitates a recession of the œdema, allows drainage in the case of possible suppuration, and also probably relieves the pain by releasing the peritoneal tension.

ECTOPIC SPLEEN CAUSING INTESTINAL OBSTRUCTION

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From the Surgical Service of the Sydenham Hospital

Ectopic or wandering spleen is a comparatively rare condition, as is indicated by the fact that in five hundred splenectomies done at the Mayo Clinic [1] there were only two cases of "wandering spleen."

Case Report.—The patient in my case was a woman, seventy-three years of age, who had been in good health for the past forty years except for four attacks of pain in

Fig. 1.—Skiagraph showing the interruption in the fecal flow in the colon caused by the pressure of the wandering spleen.

the lower abdomen, constipation, and nausea without vomiting. There had been a twenty-year interval between the last attack and its predecessor. The attacks had lasted one to two weeks, with the exception of the last, which was of only ten hours' duration.

This last attack occurred in May, 1929, and since that time the patient had lost about twenty pounds in weight, partly owing to her loss of appetite, due to fear of the pain. A fluoroscopic examination with a barium meal a few days after this attack was followed by a low-grade fever of 100° to 100.5° F. at night.

For two months previously, the patient had felt a sausage-shaped mass in the lower quadrant, which at one time during the barium meal had become quite large and tender. She had refused to submit to any operative procedure and had been treated with ice

packs by her family physician. She was admitted to the Sydenham Hospital on August 5, 1929.

On examination there was a palpable mass in the left lower quadrant in the sigmoid axis. It appeared to be sausage-shaped, was not movable, but was compressible. There were moderate abdominal tenderness and rigidity on palpation, most marked on the left side.

The X-ray examination of the colon with a barium enema showed the following:

The rectum and distal end of the sigmoid filled readily. About mid-sigmoid there was evidence of some obstruction with very definite tenderness. After a short interim the obstruction was overcome and the barium meal was seen to pass into the descending and transverse regions of the colon. During the entire fluoroscopic examination this portion of the sigmoid over an area of about three inches in length appeared extremely spastic. The film picture had the appearance of a chronic inflammatory lesion.

In view of these findings and the patient's age, a diagnosis of neoplasm of the sigmoid was made.

The laboratory tests disclosed: Urine had a faint trace of albumin, many squamous cells, many white blood cells, some clumps. Blood count on August 5: Hæmoglobin 63 per cent.; red blood cells 3,848,000; white blood cells 8,200; neutrophiles S. F. 57 per cent., B. F. 21 per cent.; S. L. 15 per cent., mononuclears 6 per cent.; basophiles 1 per cent.

On the seventh of August operation was performed under spinal anæsthesia. A left upper rectus incision revealed an ectopic, enlarged and very congested spleen surrounded by a very tense capsule. Its pedicle was twisted, and the notched anterior border of the spleen was turned downward. There were adhesions fixing the spleen to the lower ileum. The displaced spleen, weighing about 900 grams, pressed on the descending colon and the sigmoid so as to block the passage completely. The distal transverse colon and the splenic flexure were displaced downward and distended. Clamps were placed on the pedicle, the spleen separated *in situ* and then removed. There was no post-operative shock, and convalescence was smooth.

On the second day after operation, there was an arrhythmic pulse, but otherwise the patient's condition was good. The abdomen was soft and not tender; urine and gas were voided freely from the first post-operative day; there was a good bowel movement on the second day *post operationem* and a spontaneous defecation on the following day. The wound healed by primary union, and the patient was discharged from the hospital in good condition August 16.

She remained in excellent health for about two months, when she suddenly developed anuria and died.

Three blood counts were made after operation as follows:

TABLE I

Blood Counts in Author's Case

Date	Hæmoglobin percentage	Red blood cells	White blood cells	Neutrophiles		Transitionals	S.L.	Eosinophiles	Platelets
				S.F.	B.F.				
Aug. 8.....	70	4,168,000	20,000	71	12	2	14	1	..
Aug. 10....	75	4,640,000	20,000	64	14	..	12	3	..
Aug. 12....	71	4,540,000	15,000	60	11	6	..	..	408,000

The pathological report was made by Dr. A. A. Eisenberg and read as follows:

"Enlarged spleen measuring 18 by 10 by 6 centimetres and weighing 900 grams. The capsule of the spleen is considerably thickened, and the splenic artery leading to

it is also considerably thickened. On section the spleen has a nutmeg appearance, is very friable, with very distinct markings of the venous spaces.

"Histologically, the spleen shows a marked increase in the fibrous framework, the capsule is markedly thickened, the Malpighian bodies are increased in number and size in some places. In them the lymphocytes are decreased and the endothelial cells are increased proportionally. There are areas of fresh hæmorrhage present throughout. The blood spaces in the pulp are unusually dilated. Fibrosis around some Malpighian corpuscles suggests the appearance of fibro-adenoma.

"*Pathological diagnosis.*—Idiopathic splenomegaly, possibly Banti's disease?"

REVIEW OF EARLIER LITERATURE

Wandering or ectopic spleen is usually acquired and occurs more frequently in women. It is caused by traction on its suspensory ligaments and favored by enlargement of the organ with consecutive increase in its weight, and by laxity of the abdominal wall.

Torsion of the pedicle is not an uncommon complication. Intestinal obstruction due to the wandering spleen is, however, an unusual condition.

In the earlier literature there are records of five cases in which the patients died of ileus; pressure of the ectopic spleen or from its twisted pedicle was found to be the cause.

Alonzo (*Arch. d. med. espagn. y etrang.*, October, 1846) reports a case in which the spleen was found in the right iliac fossa, covered with omentum and adherent to surrounding tissues; the transverse colon was displaced by the enlarged spleen and strangulated.

Babesiu,[2] 1877, reports a case in which the patient with slight symptoms of ileus was treated with enemata, calomel and croton oil from the fourth to the thirteenth of August, 1877. The full diagnosis was made at autopsy and reads as follows: "Strangulatio ansæ jejuni per ligamentum gastro-lienale lienis migrantis dextrorsum versus tortum, subsequente thrombosi venæ et arteriæ lienalis, gangræna lienis, peritonitide et ileo." The spleen lay in the left inguinal region extending into the right side of the small pelvis. It was adherent, and the gastro-splenic ligament was twisted. A loop of jejunum was caught and compressed between this ligament and the spinal column.

In Collins' case,[3] 1882, an enlarged and displaced spleen pressed on the sigmoid flexure and caused strangulation.

Ledderhose,[4] 1890, cited a case described by Helm and Klob in which the spleen lay along the inner surface of the left ilium, the pancreas being so displaced that it pressed the duodenum up against the vertebræ, causing gastric dilatation and subsequent gangrenous perforation.

In 1893 Körte [5] demonstrated a specimen obtained at autopsy showing an ectopic spleen with a twisted pedicle. A loop of small intestine was caught and strangulated between the adhesions at the upper pole and the pedicle, causing the fatal intestinal obstruction.

REVIEW OF RECENT LITERATURE

In the more recent literature, a few cases have been reported in which a wandering spleen caused symptoms of intestinal obstruction and in which splenectomy was done with complete relief of symptoms.

O'Shea [6] in 1915 reported two cases of wandering spleen in women; one aged forty-four, the other forty.

In the first case, there had been several attacks of severe abdominal pain and

vomiting in the past eighteen months. Three days before she came under care, she had developed a similar attack of pain and vomiting with inability to secure a satisfactory bowel movement. The abdomen was tender to pressure, and there was a large, rounded, somewhat movable and tender mass in the right iliac fossa.

At operation, this mass was found to be a large and engorged spleen, twisted on its pedicle, with "a loop of the small bowel engaged in the torsion." Splenectomy was done and the patient made a good recovery. The spleen showed chronic passive congestion. The patient was in excellent health after the operation. At the last examination, eighteen months after operation, the blood count showed red cells 4,500,000, white cells 6,900, and no abnormal cells.

In the second case reported by O'Shea, there were no symptoms of intestinal obstruction. A tumor was palpable on the left side of the pelvis. Splenectomy resulted in complete recovery.

PETRIDIS [7] in 1918 reported two cases of wandering spleen with torsion of the pedicle; one in a man twenty years of age, the other in a woman thirty-two years of age.

In the first case, before admission to the hospital, there had been four days during which no fæces were passed, and the patient had considerable pain. This condition was relieved by a laxative and hot applications. On examination a tumor was found on the right side of the abdomen. This was not recognized as the spleen until operation was done. In the second case the spleen was found to be adherent to the appendix. Both these patients were treated by splenectomy and both made good recoveries.

In 1922 PACCHINI [8] reported a case in a woman fifty-six years of age. Ten years previously she had had an attack of abdominal pain and gastric dilatation with vomiting, relieved by the passage of flatus. Shortly before admission to the hospital she had one attack of abdominal pain and vomiting, and was admitted to the hospital when a second attack developed. Meteorism was so marked that abdominal palpation could not be done satisfactorily. It was somewhat relieved by the passage of a long tube into the intestine to aid the escape of flatus following the administration of an oil purgative. Then a tumor could be palpated on the left side of the abdomen, which from its form and consistency was thought to be the spleen. At operation, this diagnosis was confirmed. The mass was of globular shape but normal in size and consistency. Splenectomy was followed by complete recovery.

BROSSMANN [9] in 1922 reported a case in a woman forty-five years of age, who was sent to the hospital with a tentative diagnosis of ileus. She had had severe epigastric pain and nausea and passed neither fæces nor flatus. There were abdominal distention and tenderness to pressure on the left side, where a tumor was palpable. At operation, this tumor was found to be the spleen on a twisted pedicle and adherent to the omentum. After freeing the adhesions and ligating the pedicle, the spleen was removed. It was enlarged and showed hæmorrhagic necrosis. The patient was in excellent health two months after operation. Three blood counts on the second, fourth and eighth days showed the lowest red cell count, 4,000,000, on the fourth day; by the eighth day it had risen to 6,000,000; the total leucocyte count diminished from 17,000 to 14,000.

In 1927 HARRIS [10] reported a case of wandering spleen causing intestinal obstruction in a man twenty-seven years of age. He had not passed fæces or flatus for about thirty-six hours prior to admission; he had vomited "some greenish fluid" once. Pain was not severe, although there were occasional "colicky attacks." The abdomen was slightly distended, and there was a large, rounded, firm mass to the left of the umbilicus. The patient stated that he had noted the presence of this "lump" for about a year, but it had caused no symptoms. An exploratory laparotomy was done. A left subumbilical paramedian incision was made and "a firm, fleshy, reddish-blue mass" found that proved to be the spleen. The pedicle had undergone torsion for one complete turn. The tail of the pancreas was contained in the pedicle. The spleen was removed without difficulty; the pedicle was ligated in several portions distal to the tail of the pancreas and the free ends of the vessels invaginated. The patient died on the ninth day following a sudden

collapse. Examination of the spleen showed a misshapen organ with a high degree of passive congestion.

Harris noted that Ledomski (*Khirurg. Mosk.*, vol. xxiv, p. 559, 1908) reported a case in 1908 in which a wandering spleen with twisted pedicle caused intestinal volvulus. In his own case, Harris believed that the twisting of the pedicle acted as the predisposing cause of the obstruction, the consequent swelling of the organ sufficing to obliterate the lumen of the bowel by pressure.

Discussion.—In my own case, I am of the opinion that elongation of the ligaments with its consequent stretching of the blood-vessels, aggravated by the torsion of the pedicle, produced congestion and enlargement of the spleen, which then pressed heavily on the intestines, as in the case noted above by Harris. I am strongly of the belief that in my case the removal of the organ was the only possible procedure, and in this opinion I find myself in agreement with others. Fowler [11] states that, in cases of wandering spleen, splenectomy is the treatment of choice and produces "slight if any change in the blood picture." Sutton [12] says that the most satisfactory treatment for wandering spleen with twisted pedicle is splenectomy.

Pool and Stillman [13] write that in cases of movable spleen beneficial results should be "confidently expected" from splenectomy and that even with torsion of the pedicle, the prognosis should be good if there is "prompt recognition that a surgical condition exists."

A definite pre-operative diagnosis of ectopic spleen causing intestinal obstruction is rarely made, as indicated by the cases already cited. The spleen under those circumstances is usually palpable as a "mass" or tumor and is often enlarged and misshapen, so that its typical outline, especially the anterior notched border, cannot be recognized. The symptoms, however, indicate the need of operation.

Removal of the spleen in adults is generally recognized as entirely compatible not only with life but also with good health and vigor. The functions of the spleen are evidently taken over by other parts of the reticuloendothelial system. Following splenectomy, there is usually some change in the blood count, which may be persistent; but there is comparatively little variation from the normal and no abnormality of the blood cells.

Fowler,[11] as noted above, believes that the blood change is slight, if any, when there is no previous disease of the spleen.

Beer [14] states that, following splenectomy, there is an increase in the blood platelets and usually in the red cells; also, a tendency of the white cells toward an increase in the lymphocytes and sometimes in the eosinophiles.

Carrol Smith [15] reports a case in which splenectomy was done for a wandering spleen simulating a uterine tumor. A month after operation, the red cell count was 5,000,000; the white cell count, 7,400.

In Sutton's [12] case of splenectomy for wandering spleen with twisted pedicle in a boy thirteen years of age, the total white cell count was high, 31,700, immediately after operation. It decreased subsequently but remained above normal (14,800) six weeks after operation. There was a steady decrease in the polymorphonuclear cells and an increase in the percentage of lymphocytes, the last count showing 59 per cent. polymorphonuclears, and 40 per cent. lymphocytes. The red cells at this time had increased to 5,100,000.

HALL [16] reports a series of blood counts in a case in which operation was performed for traumatic rupture of the spleen. The white cell count was variable for the first two and one-half months after operation; then, in the last period of observation—up to three months after operation—it showed a definite leucocytosis varying from 8,700 to 13,500, averaging 11,570, with 50 per cent. of neutrophiles and 40 per cent. of lymphocytes. From his study of the white cell count in this case, including the Arneth index, he came to the conclusion that the increase in the leucocyte count after splenectomy is due in part to the removal of some factor that restricts the production of white cells—possibly a function of the normal spleen.

LARRABEE [17] also notes that after splenectomy for ruptured spleen there is a persistent leucocytosis with a relative increase in lymphocytes and endothelial cells. These slight variations from the normal in the blood counts, however, do not appear to have an effect on general health, as all the patients in these cases are reported as in full health and vigor.

SUMMARY

1. An unusual case of ectopic spleen is reported. The organ occupied the left lower quadrant of the abdomen, in the sigmoid axis, and pressed upon the descending colon and sigmoid so as to cause intestinal obstruction. Its pedicle was twisted. Splenectomy was performed. The patient made a good recovery; but, two months later, she suddenly developed anuria and died.

2. A survey of the literature proves that such cases of wandering spleen with twisted pedicle causing intestinal obstruction are of rare occurrence.

3. The pre-operative diagnosis of the underlying cause of the intestinal obstruction in such cases is exceedingly difficult, even impossible, on account of the pathological changes occurring in the spleen, disfiguring its outline.

4. Authorities agree that splenectomy is the operation of election.

5. Following removal of the spleen, there is generally rapid improvement in the hæmatologic condition.

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INTESTINAL OBSTRUCTION

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The problems involved in the not infrequent occurrence of intestinal obstruction and the distressingly high percentage of mortality have in the past, as even in the present, given great incentive to repeated studies and experimental work of the fundamental questions underlying the whole subject of intestinal obstruction. The illustrious work done in American laboratories of late years in experimental obstruction has been of immense value in guiding the surgeon through his prognostic as well as therapeutic ideas. In the last quarter of the nineteenth century the mortality statistics have approximated 90 per cent. Today the large clinics are reporting decided improvements over this. Van Beuren and Smith[1] record a mortality of 42 per cent. in a series of 1000 cases. In a selected series of cases W. B. Holden reports a very low mortality.[2] A better understanding of the causes responsible for death in intestinal obstruction has paved the way for rational pre-operative and post-operative care. The recognition that early diagnosis is essential for immediate surgical intervention has been an important factor in the treatment of intestinal obstruction. Surgeons today should be firm in the belief that to watch and wait is more than dangerous—that to look and act means the saving of life. Many investigators have, from time to time, advanced numerous theories for the causation of death from intestinal obstruction.

Etiology.—Among the more important considerations are: (1) The belief that the mortality in cases of intestinal obstruction was due to a nervous reflex. The sympathetic system at one time was responsible for all ailments. It is therefore not at all surprising to note that the cause of death in intestinal obstruction was credited to the autonomic system. Volvulus was thought to produce a disturbed sympathetic mechanism simulating surgical shock. Localized irritation of the vegetative system does not result in the morbid picture as is in evidence in obstructed intestinal patients. We can readily dismiss the neuro-reflex consideration.

(2) With the advent of new concepts and knowledge of the behavior of organisms, the bacterial cause was presented. The thought was expressed that the body was invaded by bacteria from the damaged bowel. This would well explain that group complicated by peritonitis. Bacteria might reach the blood-stream. Cultures, however, taken from the liver, spleen, and other organs have been invariably sterile. More recently attention and interest have been drawn to the work of Copher, Stone and Hildreth[3] and their studies of intestinal obstruction as it is related to Bacillus Welchii. Their

investigations would point to a relationship of Bacillus Welchii and intestinal obstruction. They have reported an experimental series of fourteen dogs treated with Bacillus Welchii antitoxin, in which four recovered. Their results are not impressive. We do not believe, however, they are themselves willing at this time to be conclusive in the bacterial background for intestinal obstruction. McIver, White and Lawson,[4] in a series of investigating experiments, definitely conclude that while Bacillus Welchii may be found in enormous numbers in a portion of obstructed bowel, there is some other and more important factor at work. Caution is urged in accepting the importance of Bacillus Welchii as an agent in intestinal obstruction and the use of antitoxin of Bacillus Welchii or any other serum must continue to be considered in its experimental stage.

(3) The more recent, and undoubtedly most reasonable, explanation lies in the toxin-chemical theory. There is an absorption of some toxic substance from a portion of the bowel, the route of absorption being through the vascular system—less likely through the lymphatics. Scholefield[5] has successfully demonstrated the monumental fact; namely, that when mice are injected intraperitoneally with portal blood or serum from artificially obstructed dogs, there is an invariable fatality to the mice. Systemic blood, when used, resulted in no untoward effects or obstruction manifestations. The latter may be due to the detoxifying action of liver. Fluid when taken from the lumen of obstructed bowel was of no effect when administered by mouth or injected into the bowel or intestine. The site of formation of this toxin is, of course, important, particularly to the surgeon, as to his treatment. It is quite possible, as Scholefield surmises, that the formation of the toxin within the limits of an obstructed bowel is due to a three-fold cause: bacteria, a necrosing mucosa, and increasing intra-intestinal pressure. The element of time must elapse before conditions are favorable for the toxin passing into the blood-stream.

The toxin.—The nature of this toxin has been described by Stone and his co-workers[6] as a substance resembling proteose—this intestinal substance after it has been precipitated with 95 per cent. alcohol and later specially prepared could be injected into dogs, producing the symptom complex and death, as is seen when fluid from a loop of obstructed bowel is injected. The presence of pain, vomiting, fall in blood-pressure and later collapse are in evidence. Katzenelbogen,[7] in a recent contribution, again brings to our attention the rôle that proteose-like bodies play in intestinal obstruction. These bodies, when injected either subcutaneously or otherwise, have a very pronounced stimulating action on the gastric secretion and chiefly on the secretion of free hydrochloric acid. These facts are of great importance in the acceptance of the toxin basis of fatality in intestinal obstruction, for, as will be seen later, the altered blood chemistry findings can then be well explained. This demonstration of a harmful substance in the blood from an obstructed loop of bowel is fundamental and paramount. It strongly con-

firms the validity of a toxin as being basic in the mortality of intestinal obstruction.

Chemical manifestations of blood.—Repeated studies of the chemistry of blood in intestinal-obstructed patients constantly reveal: (*a*) increased non-protein nitrogen; (*b*) fall in blood chlorides; (*c*) elevation in the carbon-dioxide combining power of the plasma. The increased non-protein nitrogen content as Haden and Orr[8] explain is due to: (1) blood plasma concentration resulting from a marked diminution in body fluids; (2) evident tissue destruction. The fall in chlorides is plausibly reasoned to be due partly to a loss of chloride as hydrochloric acid through persistent vomiting. Dragstedt[9] has advanced the thought of the toxin eliberated in obstructed patients as producing marked stimulation in gastric-pancreatic and intestinal secretions. Experimental evidence is therefore in accord with our belief of a toxic substance generated in intestinal obstruction—which toxic substance is causative of the disturbed physiology evidenced in the characteristic blood chemistry of obstructed patients.

COMPOSITION OF NORMAL BLOOD AND OF THE BLOOD IN CERTAIN PATHOLOGICAL CONDITIONS*

Special Reference to Intestinal Obstruction

	Normal	Chronic Nephrites	Diabetes	Uremia	Intestinal Obstruction
Non-protein nitrogen, Mg. per 100 cc.	25–35	35–90		90–350	35–90
Alkali reserve cc. of carbon-dioxide in 100 cc. plasma..	77–53				100–77
Chlorides as NaCl—per cent.	0.65	0.55–0.75	0.60	0.45–0.65	0.15–0.4

* Hawk, P. B.: Physiological Chemistry, Saunders.

SYMPTOMATOLOGY

It is unnecessary here to relate the detailed symptoms as are encountered in intestinal obstruction. A good history is essential. It should be focused towards previously complained abdominal pain. The tell-tale scar or scars of previous operations should be carefully investigated, whether or not a "clean" or drainage case. The elimination of hernia—incisional, acquired, congenital, strangulated or incarcerated. Persistent vomiting, abdominal rigidity and obstinate constipation are late signs. This triad is suggestive of trouble. The diagnosis is often difficult. A careful and painstaking history with coöperation of the laboratory and röntgenology departments will be of great assistance. As an example I can cite the case of a woman, aged seventy, who had suffered from obstinate constipation for several years, associated often with vomiting, at no time of a stercoraceous character. The patient had become extremely emaciated and weak. She finally was unable to retain food or even liquids. There was marked abdominal distension. The clinical impression was one of intestinal obstruction. Röntgen-ray study revealed nothing of importance. It did however exclude cancer, adhesions, mesenteric thrombosis, volvulus, strangulation and intussusception. The blood chemistry

showed twenty-eight millimetres non-protein nitrogen and .45 per cent. chloride. The clinical diagnosis finally reached was that of paresis of the bowel, the plexus of Meisner and Auerbach being affected. Proper therapeutic measures were instituted immediately, consisting of enemata, Rochelle salts by mouth and turpentine stupes to abdomen. The patient made an uneventful recovery and left the hospital able to retain food, and with the disappearance of any abdominal distension. The importance of a careful history, laboratory and radiographic studies is therefore evident.

Intestinal obstruction, according to Charles Mayo[10] would fall under the following category: (*a*) the apparent obstruction, really due to intestinal stasis; (*b*) obvious hernia; (*c*) acute obstruction from an intra-abdominal lesion; (*d*) post-operative obstruction. Foster[11] from a physiological viewpoint classifies the obstruction: (1) the simple obstruction, with no evidence

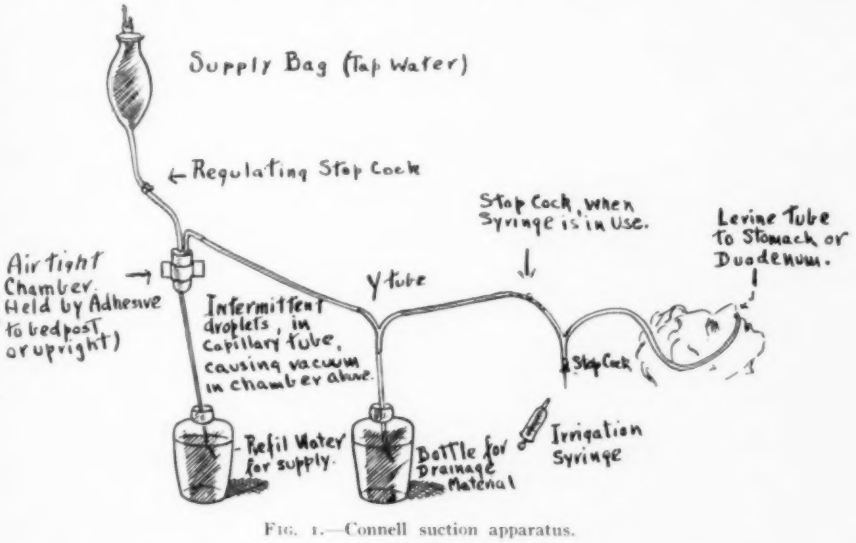
Supply Bag (Tap Water)
← Regulating Stop Cock
Stop Cock, when Syringe is in Use.
Levine Tube To Stomach or Duodenum.
Air tight Chamber (Held by Adhesive to bedpost or upright)
Y tube
Intermittent droplets, in capillary tube, causing vacuum in chamber above.
Stop Cock
Refil Water for supply.
Bottle for Drainage Material
Irrigation Syringe

FIG. 1.—Connell suction apparatus.

of vascular derangement; (2) the acute intestinal strangulation where the vascular supply is grossly interfered with; (3) the physiological obstruction. We have used the grading of intestinal obstruction: Grade I, the simple obstruction with normal blood chemistry; Grade II, the obstruction with strangulation and a moderate change of non-protein nitrogen and chloride content of the blood; Grade III, obstruction with strangulation and presence of stercoraceous vomiting and marked increase in non-protein nitrogen content and marked diminution in chlorides of blood. It is paramount to emphasize the importance of early diagnosis. The surgeon prefers to find little or no pathology in his exploratory operation rather than to encounter too much.

Pre-operative management.—The results of pre-operative care of intestinal obstruction have been excellent. Early diagnosis is essential. Once the presence of intestinal obstruction is recognized, immediate treatment is to be instituted. The introduction of sodium chloride, by mouth, by rectum,

subcutaneously and intravenously. The amount used is chiefly governed by the type of obstruction. The normal saline solution is used intravenously, a 3 per cent. solution has been found efficacious. The intravenous infusion may be repeated during the day, chiefly being governed

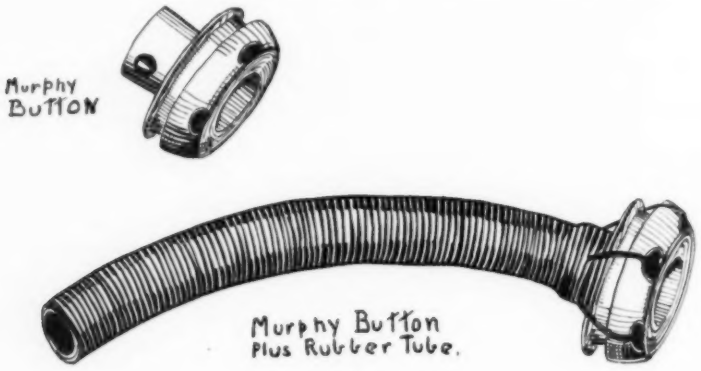

FIG. 2.

by symptoms and progress. The use of glucose intravenously and rectally is beneficial. Without subjecting the patient to any unnecessary pain or further risking the margins of safety, withdrawal of blood for chemical analysis may be done. Cathartics and food by mouth are contra-indicated.

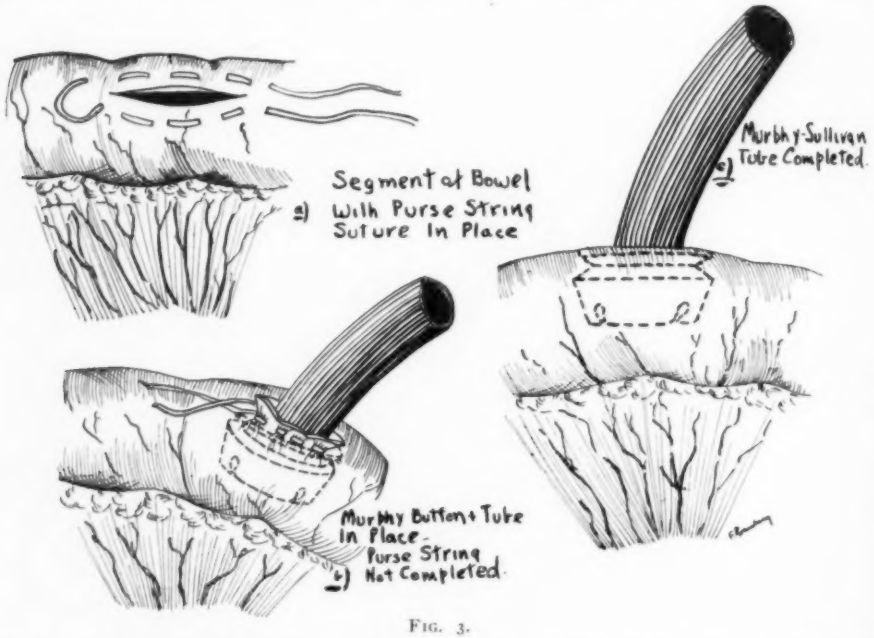

FIG. 3.

Where abdominal distension is in evidence, and the time limit can be overlooked with certainty, measures to alleviate or combat this condition can be considered. We have found the turpentine stupe, the flaxseed poultices, or common heat of benefit. The use of pituitrin or eserin is dangerous.

Enemata with the patient in the knee-chest position are highly beneficial, the types used frequently being the milk and molasses, olive oil, hydrogen peroxide, and barium.

Dr. P. F. McPartland, working with the Connell Suction (Fig. 1) has had excellent results with its use in obstructed patients.[12] In our pre-operative armamentarium of obstructed patients, the use of the Connell suction is valuable.

In patients presenting the diagnosis of intestinal obstruction who are poor operative risks, the use of saline intravenously, glucose and saline per-rectum, stimulatory medication, and, lastly, the introduction of the Connell suction will be life saving and greatly reduce the mortality in an otherwise fatal condition.

Surgery.—It is therefore evident that surgical interference in intestinally obstructed cases must be preceded by a careful consideration of the foregoing facts. A lengthy operation may prove too great a tax on an already rapidly diminishing margin of a patient's resistance. The spinal route in experienced hands is the anæsthesia of choice. Nitrous oxide or regional infiltration may be used. The site of incision should correspond to the more common areas of obstruction; namely, appendiceal, hepatic or sigmoid. A rapid exploration may be done to quickly determine the point and cause of the obstruction. Whether to remove or correct the cause should be tempered with caution, with the life of the patient at stake. After the storm has passed removal of the obstruction causes may be considered. A too sudden release of obstruction may cause death. In moderately mild obstruction cases specific surgery is indicated. But unfortunately we do not often encounter the early obstructed case. They come to us when the diagnosis has been made late, where the time element has elapsed sufficiently to allow absorption of the toxin. The incision is made at one of the points above mentioned. Clear odorless fluid emerges; this would indicate early peritoneal effusion, a good omen; the gushing of sanguinous fluid would mean serious trouble ahead, especially if foul. A "knuckle" of gut forces itself out of the wound—it is this segment that is "crying" for relief. The method of treatment at this stage, which, in our hands, has yielded very gratifying results, is basically one of drainage. The senior author has used for several years the Murphy button plus an attached rubber tube. (Figs. 2, 3, 4.) This is done rapidly. The soil-

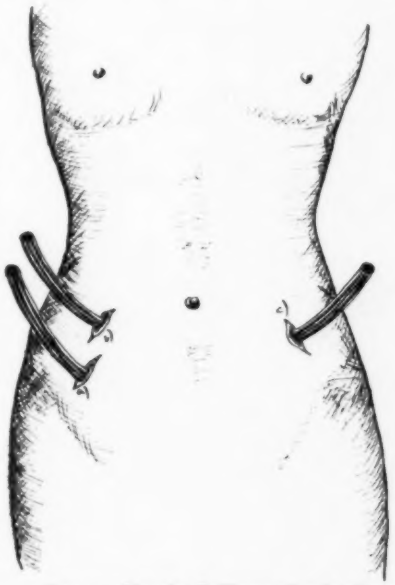

FIG. 4.—Murphy Sullivan tubes in place. Abdomen closed. Points of usual obstruction. (a)—Appendical. (b)—Hepatic. (c)—Sigmoid.

ing of the operating field is thus prevented, and a later peritonitis is thus minimized. The precautions against peritonitis are essential, for mortality in obstructed cases rises rapidly and is a real menace. Similar incisions and insertions of Murphy Button tube are advisable in other portions above the obstructed bowel. When the tubes are in place, irrigation with normal saline solution is effected. This is continued until the solution comes through the tubes clear. The patient is now given sodium chloride 3 per cent. intravenously, glucose and salines rectally. Supportive stimulation is advisable. The Connell suction may be used to advantage at this time. When the patient has been brought out of danger, when the pulse, respiration and temperature are in normal limits, and when the patient presents an operative risk, further exploratory, removal of Murphy Button tubes and causes of obstruction may be undertaken.

SUMMARY

1. In the light of recent experimental work it seems most probable that a toxic substance produced in the obstructed bowel is responsible for the grave symptoms and death.

2. The dissemination is by way of the portal blood stream.

3. Pre-operative and post-operative introduction of salines through all channels.

4. The use of the Connell suction.

5. Early diagnosis and surgery paramount.

6. Use of Murphy-Sullivan tube of great benefit.

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THE USE OF PERFRINGENS ANTITOXIN IN INTESTINAL OBSTRUCTION

AN EXPERIMENTAL STUDY*

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In 1926, Williams[1] reported favorable results from the use of bacillus Welchi (perfringens) antitoxin in patients suffering from intestinal obstruction. He reported a reduction in the operative mortality of a series of cases treated with this antitoxin to 9.3 per cent. in contrast to one of 24 per cent. in a series of cases which were not given perfringens antitoxin. Such a striking reduction immediately called this work to the attention of other surgeons. Bower and Clark[2] and others have also reported favorable results following its use in patients.

Recently, experimental evidence has been advanced which would confirm Williams' findings. Morton and Stabins[3] found that, in dogs, the development of the toxæmia following obstruction in the jeunum seemed to be delayed by the administration of the antitoxin and the mortality was lower in animals given perfringens antitoxin previous to operative relief. Copher, Stone, and Hildreth[4] utilized an isolated closed loop of the jejunum and concluded that the administration of the antitoxin prolonged the life of the animals. Unfavorable reports following the use of perfringens antitoxin in experimental obstruction have come from McIver, White, and Lawson,[5] who were unable to demonstrate any beneficial effect from the antitoxin when given to cats having jejunal obstruction and from Owings and McIntosh,[6] who studied obstruction of the jejunum in dogs. Our results, are similar to those reported by these authors.

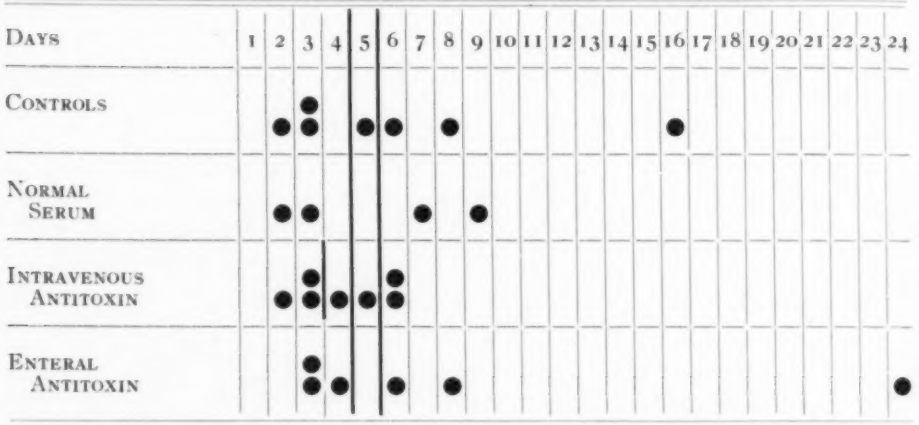
Method. Our work was undertaken in the hope of securing additional confirmation from the experimental laboratory of the exceedingly promising results obtained by Williams. An attempt was made to simulate as closely as possible the usual type of intestinal obstruction encountered in the clinic. The experiments cited above have dealt without exception with high intestinal obstructon. Actually, the preponderant number of cases present obstruction at a lower level, usually the lower ileum or colon. The two types are distinct. High obstruction is characterized by excessive vomiting with resultant or concomitant depletion in blood chlorides, alteration of base and nitrogen retention. There is a very rapid lethal termination in untreated cases. Alterations in the chemistry of the blood are not conspicuous when the obstruction is in the lower bowel and dogs with this type of occlusion do not vomit. Accordingly, we chose a uniform low level for the production of obstruction; namely, six inches above the ileo-cæcal juncture. In addition to simulating closely the common type of clinical obstruction, this procedure provided an obstructed segment of bowel which afforded a favorable media for the growth of anærobic organisms, normally found in greater numbers in the more distal segments of the intestinal tract.

* From the Laboratory of Research Surgery and the Department of Surgery (Division C) of University of Pennsylvania. The H. K. Mulford Laboratories supplied the antitoxin used in these experiments.

A simple occlusion by section and inversion of the stumps was chosen in preference to more complicated or artificial procedures such as strangulation occlusion or isolated loop. The anæsthesia for all operations was sodium amytal injected intraperitoneally. The dosage was fifty milligrams per kilo of body weight. The technic involved a section of the ileum by the cautery between clamps at the definite level noted. The stumps were then inverted by silk sutures according to the aseptic method of Kehr. Any laceration of the mesentery was repaired. In interpreting results, only those animals were considered for which no cause of death, other than toxæmia, was apparent at autopsy. The dogs that died from peritonitis or other accidents incident to the operation were excluded. It is unfortunate that autopsy protocols were not reported in some of the previous studies. Every animal in this study was autopsied shortly after death. Food and water were given the animals but they rarely ate.

Results.—A group of seven dogs served as a control. These survived for two, three, three and one-half, five, six, eight, and sixteen days respectively. The average was 6.2 days. The wide range in the duration of life, in this as well as in the other groups, will be commented on later.

Survival Period After Obstruction



A second control group of four animals served to test the specificity of the antitoxin under consideration. These dogs were given fifty cubic centimetre of normal horse serum intravenously at the time the obstruction was produced. The average duration of life in this series approximated very closely that of the first group, namely 5.8 days.

Seven animals were then given perfringens antitoxin (Mulford) fifty cubic centimetre intravenously, at the time of the operation, so that each animal received a dose which would neutralize 62,500 minimum lethal doses of perfringens toxin. These animals lived from two to six days or an average of 4.1 days.

Finally, the antitoxin, 62,500 minimum lethal doses, was injected directly into the obstructed loop of ileum. Six animals had an average survival period of eight days. There is included in this group, however, a remarkable animal which appeared emaciated but quite healthy twenty-four days after operation. He was killed and found to have a completely obstructed bowel. Unfortunately, no cultures were made in this dog. If this exceptional animal is omitted, the average for the group becomes 4.8 days, or approximately the same as that in which the antitoxin was given intravenously.

Comments.—The variability in the effects produced by obstruction at a given level and by a uniform technic was noteworthy throughout the experiments. The duration of life varied from two to twenty-four days. The

pathological changes were likewise inconstant. A separate series of five animals was re-operated on the fifth day, the obstruction being relieved at this time. One animal showed dilatation of the bowel for a distance of not more than twelve inches above the obstruction and very slight œdema of the intestinal wall. In another there was distention and œdema of the entire proximal segment as far as the duodenum and, in addition, purplish blotches of impending gangrene along the anti-mesenteric border. The lesions in animals observed at autopsy varied from moderate uniform distention of the obstructed segment to a dilatation four times the normal calibre and gangrenous perforation. Moreover, it was found to be impossible to predict from the appearance of the animals from day to day when death might occur or the nature of the pathology which would be encountered at post-mortem. In several instances an animal was observed walking about its cage only four or five hours before its death. Pulse acceleration generally accompanied toxæmia. However, several animals lived for two or three days with pulse rates of 180 or more. Others did not at any time have rates exceeding 120. Alterations in the chemical constituents of the blood cannot be used as guides to the degree of toxicity in low obstruction as pointed out previously. Morton and Stabins used these as an index of toxicity in their animals with jejunal occlusion. Their proctocols, however, indicate that, even in high obstruction, these alterations occur late and are somewhat inconstant.

Bacteriological studies.—During the early part of this experiment, an attempt was made to correlate the rate of proliferation of the anærobic organisms in the bowel with the development of toxæmia. The method involved refrigeration of samples of intestinal contents for twenty-four hours to promote sporulation, heating to 80° for ten minutes to destroy all vegetative organisms and inoculation into litmus milk. Imperfect, but satisfactory, anærobiasis was produced by keeping the media at 90° for thirty minutes and overlaying the cultures with paraffin oil. After forty-eight to ninety-six hours of incubation, the presence in the culture of anærobic, spore-forming, gas-producing organisms of the perfringens group was determined by the odor of butyric acid and the characteristic stormy fermentation of the milk with shredding of the coagulum and gas bubbles. In twenty-two animals cultured at the time and at the site of obstruction, eleven showed positive growth of organisms of the perfringens group.

A series of five dogs, not included in the previous summary of results, was re-operated on the fifth day. From the obstructed segments of these animals, material was obtained for a rough quantitative measurement of the degree of proliferation of the organisms after obstruction. This was done by the inoculation into culture media of varying dilutions of the intestinal contents. Growth was never found in dilutions higher than one to ten at the time of production of the obstruction. All four animals from which cultures were obtained on the fifth day showed marked proliferation of organisms in the obstructed bowel. Two showed growth in dilutions of 1 to 1000 and two

others in 1 to 10,000 dilution. Post-mortem cultures were not considered since agonal changes render such evidence unreliable.

CONCLUSIONS.—Throughout this study we have been impressed with the need for extreme caution in drawing definite conclusions. Ample evidence of the extreme variations encountered has been presented. It appears that the anærobic, sporulating, gas-forming organisms of the perfringens group are frequent inhabitants of the terminal ileum of the dog. Moreover, they proliferate in the lumen of the bowel following obstruction. Nevertheless, the use of the antitoxin both intravenously and enterally has not provided us with any evidence that it exerts a deterrent influence upon toxæmia or prolongs life following the production of low intestinal obstruction closely simulating that encountered by the surgeon. It may well be that giving the antitoxin, as we did, in a single dose at the time the obstruction was produced, did not render it available to the organism at the time it was most needed. Repeated administration might conceivably exert a more favorable influence, but Owings and McIntosh could not confirm this. Furthermore, a variation in the strain of the organisms concerned may account for the different results obtained by Williams.

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THE PREVENTION OF PERITONEAL ADHESIONS BY AMNIOTIC FLUID*

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Ever since the advent of aseptic surgery, the occurrence of adhesions after abdominal operations has presented a serious problem to the surgeon. The literature is replete with suggestions as to how these may be prevented, but as yet I know of nothing which has been offered which is really of any great usefulness in the majority of instances. Many articles, each supposedly fruitful, in its offerings, have appeared, only to be followed by less favorable reports from other investigators, who were unable to confirm the original findings. The mere number of substances recommended is mute evidence that none is entirely satisfactory.

Kubota[1] made an exhaustive review of the literature from 1880 to 1924. He carried out a series of investigations with a papain extract and a substance called Koktol. With both of these substances he had a measure of success. Since his investigation nothing striking was reported until 1927, when Johnson [2] reported extremely favorable results following the use of amniotic fluid. Johnson's observations find confirmation in the work of Warren[3] and Trusler,[4] although the later author has not as yet published his data for critical analysis.

The etiology of peritoneal adhesions has been studied from many angles. Cheatle[5] classifies adhesions under two types: (1) direct, in which two opposing denuded surfaces come in contact and heal by first intention; and (2) indirect, in which long strands of fibrin become organized by replacement with connective tissue which is covered by endothelium. Fromme[6] states that if the peritoneum is traumatized under the strictest aseptic precautions, no adhesions will result. It cannot be denied that in all probability infection plays a definite rôle in all peritoneal adhesions but experience has taught us that with the best aseptic precautions adhesions will result in a portion of the cases where laparotomy is performed.

Several interesting aspects of this problem have presented themselves. A perusal of case histories at the Hospital of the University of Pennsylvania has revealed several cases where extensive adhesions present at one operation had, to a large extent, disappeared at a subsequent laparotomy. Thus adhesions may, under certain conditions, disappear spontaneously. Naumann[7] has observed that adhesions are often absent some time after recovery from an exudative purulent peritonitis. He believed that biologic ferments are responsible for their absorption. Buchbinder[8] utilized repeated injections of hypertonic glucose to prevent encapsulation and plugging of drainage tubes. He noted that this solution prevented the formation of adhesions between loops of gut. On the other hand, David and Sparks[9] showed that

* Read before the Philadelphia Academy of Surgery, March 3, 1930.

the interference with the plastic exudate which resulted when glucose was used permitted bacteria to pass through the serosa and thence into the lymphatics and blood-stream.

Johnson,[2] reporting his work with amniotic fluid, described its action as due to the immediate production of a protective layer of fibrin over the

FIG. 1.—Photograph in situ of post-mortem, Dog No. 1. Control: Two enterotomies without Amniotic fluid. Hemostate in centre is attached to an adhesion at the site of one enterotomy.

injured peritoneal surfaces followed by complete resolution of the fibrin. He stated that it prevented peritonitis by the rapid production of a fibrinous

FIG. 2.—Photograph of both enterotomies in Dog No. 2. Control: Note adjacent loops adherent to sites of enterotomy.

wall with an accompanying moderate local leucocytosis. Permanent adhesions are prevented by rapid resolution of the plastic exudate through the action of proteolytic ferments resulting from the local leucocytosis. In a control series of guinea pigs in which the serosa of the intestine was

rubbed with gauze, Johnson[2] obtained dense adhesions in 100 per cent. of the animals. When boiled amniotic fluid was used, adhesions resulted in 60 per cent. of his animals, while when sterile unboiled amniotic fluid was used, he obtained adhesions in only 20 per cent. of the animals. In a later report, Johnson[10] states that subsequent investigations showed that 33.3 per cent. of his treated animals were completely protected from adhesions; 33.3 per cent. showed adhesions which were at least 50 per cent. less than his controls; while the final third were protected less than 50 per cent. over the controls. Johnson[10] has used the fluid in human cases subjected to laparotomy and has in a number of instances had the opportunity of observing the peritoneal reaction at a subsequent operation. He reported extremely gratifying immediate and late results following its use and believes that the

FIG. 3.—Photograph of enterotomy sites, Dog No. 3. Treated wth amniotic fluid.

post-operative course is smoother when amniotic fluid is used than when it is not used.

Warren[3] has reported results similar to those of Johnson.[2] His controls showed dense adhesions in 78 per cent. The operative mortality in this group was 11 per cent. With amniotic fluid, 87 per cent. of his animals had slight or no adhesions, while 12 per cent. had moderate or dense adhesions. In this group there was no operative mortality. In another series he injected iodine with and without amniotic fluid into the peritoneal cavity. The guinea pigs having iodine alone showed 100 per cent. with adhesions while those having iodine and amniotic fluid had moderate or dense adhesions in only 24 per cent., while 75 per cent. had no adhesions. Amniotic fluid, according to Warren,[3] decreases the oozing from tissues which lessens the amount of blood and fibrin and therefore reduces the probability of adhesions. He states that the fluid is slowly absorbed and thus acts as a lubricant between eroded surfaces.

Trusler's[4] data has not as yet been published so that his exact results are not available, but from a preliminary report we are led to believe that while

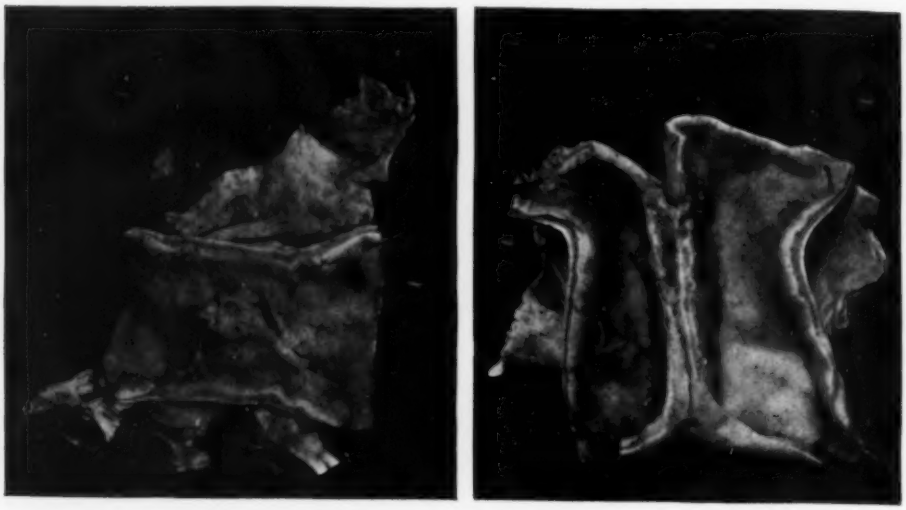

FIG. 4.—Photograph of same specimens as in Fig. 3. Intestine opened, showing the healing of the enterotomy and fusion with adjacent loop of gut.

his results were not as favorable as those of Johnson[2] and Warren[3] they were, nevertheless, encouraging. Trusler[4] does not believe that the amniotic

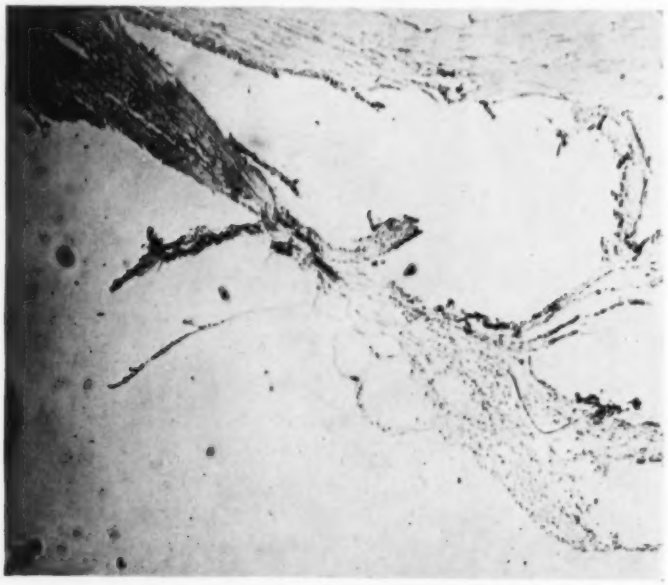

FIG. 5.—Microphotograph of a section of enterotomy of Dog No. 3. Showing adhesions to muscle layer. Treated with amniotic fluid.

fluid dissolves adhesions but that it probably stimulates the peritoneum to a more powerful defense reaction and that it stimulates a more rapid proliferation of the endothelial cells.

The work already published, however, led us to believe that at last the long-looked-for preparation had been obtained, and, with this in mind, we decided to repeat certain of the work already done in an effort to observe whether or not these findings could be confirmed in repeated investigations. The amniotic fluid used was kindly supplied by the Eli Lilly Laboratories, of Indianapolis.

We were interested in two aspects of the problem. First, we wished to ascertain whether or not adhesions subsequent to trauma could be prevented in a series of animals treated with amniotic fluid in contrast to those which we knew would result in a control series from the type of trauma to be used. Second, we were anxious to know whether or not protective adhesions which assist in the recovery from an infectious process would be formed when amniotic fluid was introduced.

Experiments.—All operations were performed under sodium amytal anæsthesia which was injected intraperitoneally. A control series of rats was injected with sodium amytal in order to ascertain whether or not adhesions would result after its use. A large number of injected rats satisfied us that sodium amytal given intraperitoneally does not cause peritoneal adhesions. Rigid aseptic technic was used in the operations. Thirty-five rats and seven dogs were studied. Six types of procedures were employed, using separate controls for each group.

TABLE I—16 RATS

Scarification of intestinal serosa

	Number of Rats	Number of Adhesions	Filmy Adhesions	Firm Adhesions
Control	3	0	1	3
Amniotic fluid	8	0	0	8

One of the control rats showed both filmy and firm adhesions.

Note.—Five rats died within twelve hours of operation and were not autopsied.

In the first group (Table I), sixteen rats were subjected to laparotomy and a number of areas of the small intestine, about one centimetre long, were subjected to scarification with a knife blade until oozing occurred. Three were closed and kept as controls. In the remaining thirteen animals, five cubic centimetres of concentrated amniotic fluid (Eli Lilly and Companys) were placed in the peritoneal cavity just before introducing the final peritoneal sutures.

The surviving rats in this group were killed after a lapse of two months. We were unable to differentiate the autopsy specimens of the controls from those treated with amniotic fluid.

In the second group (Table II), six rats were subjected to even greater trauma. The entire small intestine and cæcum were rubbed with gauze until the serosa oozed quite freely. Three animals were used as controls and in three amniotic fluid was introduced as before. The surviving animals were killed in from fourteen to seventeen days. In one control and two treated animals the entire mesentery had contracted upon itself giving the appearance of being too short for its gut. One control died in twenty-four

hours and showed very fine filmy adhesions. One treated rat died in twelve hours without demonstrable adhesions. It is believed that these two mortalities were due to the severe trauma to the gut and mesentery.

TABLE II—6 RATS

Maximum trauma to serosa

	Number of Rats	Number of Adhesions	Filmy Adhesions	Firm Adhesions	Mortality
Control	3	0	2†	1	1
Amniotic	3	1*	1	1	1

* Died twelve hours after operation.

† One rat died within twenty-four hours after operation.

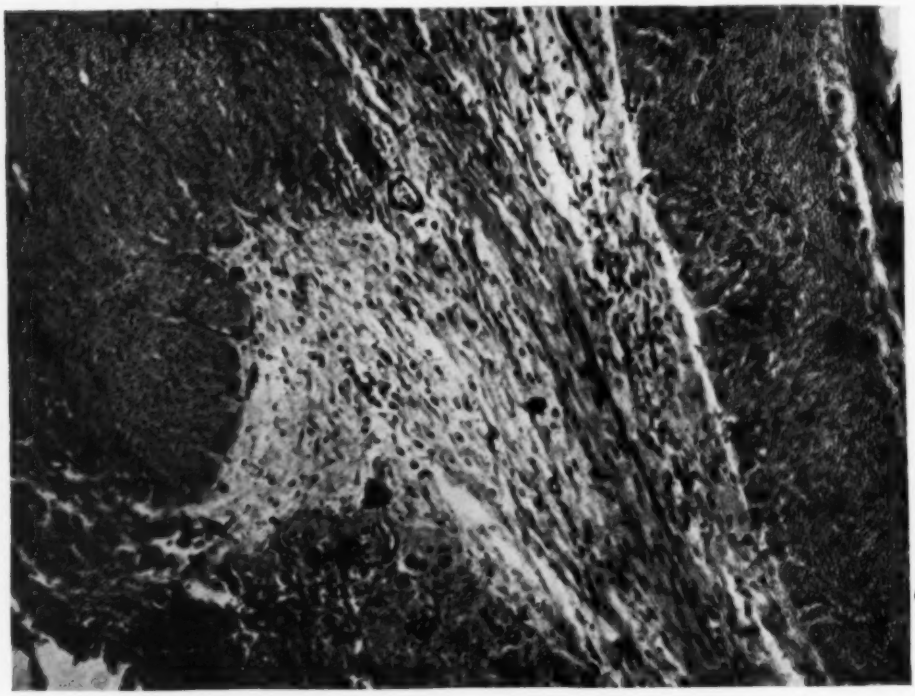

FIG. 6.—Microphotographs showing a dense adhesion between the two fused loops shown in Fig. 3.

In the third series (Table III), six rats were subjected to minimum trauma. Three points of one-half centimetre length were rubbed with gauze and in three rats amniotic fluid was injected as before. These animals were killed in from ten days to two weeks. Each of the treated rats had one or more firm adhesions.

TABLE III—6 RATS

Minimum trauma to serosa

	Number of Rats	Number of Adhesions	Filmy Adhesions	Firm Adhesions	Mortality
Control	3	0	1	2	0
Amniotic fluid	3	0	0	3	0

In the fourth group (Table IV), chemical peritonitis was produced by means of one cubic centimetre of 2 per cent. tincture of iodine injected introperitoneally without opening the abdomen. Two rats thus treated constituted the controls and in four other rats, five cubic centimetres of amniotic fluid were injected together with the iodine which was therefore diluted. The two controls died within twenty-four hours and at autopsy showed the typical picture of chemical peritonitis with many filmy adhesions. One treated animal died in twenty-four hours and showed a less severe peritoneal reaction, but it also had many fine filmy adhesions. Another treated animal died in forty-eight hours. It had a marked peritoneal reaction and many definite filmy adhesions. The remaining two treated rats recovered from their peritonitis and were killed on the fifth post-operative day. Both still showed some peritoneal reaction and one showed multiple filmy adhesions while the last was entirely devoid of adhesions.

FIG. 7.—Photograph of two enterotomy sites of Dog No. 4. Treated with amniotic fluid. This animal was entirely free from peritoneal adhesions.

TABLE IV—6 RATS

Chemical peritonitis (2% iodine)

	Number of Rats	Number of Adhesions	Filmy Adhesions	Firm Adhesions	Mortality
Control	2	0	2	0	2
Amniotic fluid	4	1	3	0	2

Two of the treated rats survived the peritonitis

In the fifth group (Table V), an attempt was made to ascertain the time of, and the mode of formation of adhesions after repeating the procedure used in group III. Three rats were used as controls and three were treated with amniotic fluid. One each of the controls and the treated rats were killed at the end of twenty-four, seventy-two and one hundred and twenty hours. The grading of the findings were found to vary with different observers, who were asked to examine the specimens and there is probably very slight difference in the controls and treated animals.

TABLE V—6 RATS

Time of Formation of Adhesions

	Number of Rats	Twenty-four Hours	Seventy-two Hours	One hundred and twenty Hours
Control	3	Filmy	Filmy	Firm
Amniotic fluid	3	Less filmy	Filmy	Less firm

In the sixth series (Table VI), the effect of amniotic fluid after intestinal surgery was studied. In seven dogs simple enterotomies were performed in two places in the small gut and closed with chromic catgut. Two dogs were used as controls and in the

remaining five, twenty-five cubic centimetres of amniotic fluid (concentrated) were introduced into the peritoneal cavity just before closure. These animals were killed six

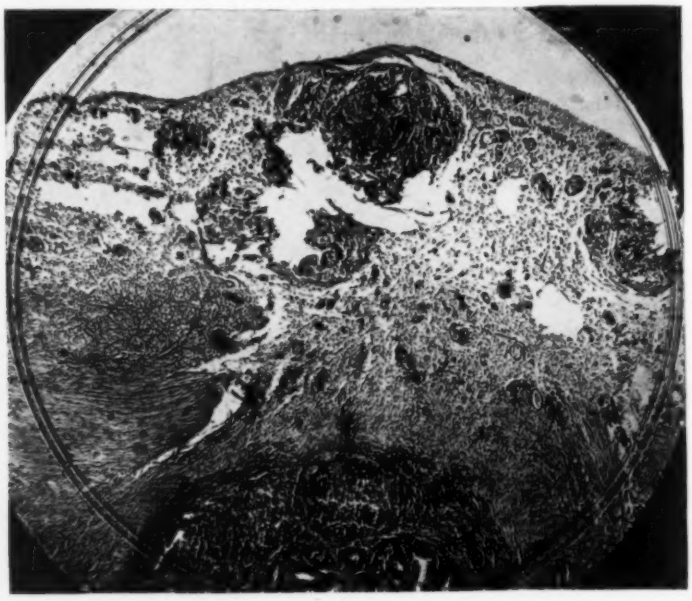

FIG. 8.—Microphotograph showing the healing of the enterotomy site shown in Fig. 7.

to eight weeks after operation. Both controls showed both filmy and firm adhesions. In one dog treated with amniotic fluid there was entire absence of adhesions and in two

FIG. 9.—Photograph of dense adhesions between two loops of gut in Dog No. 6. Treated with amniotic fluid.

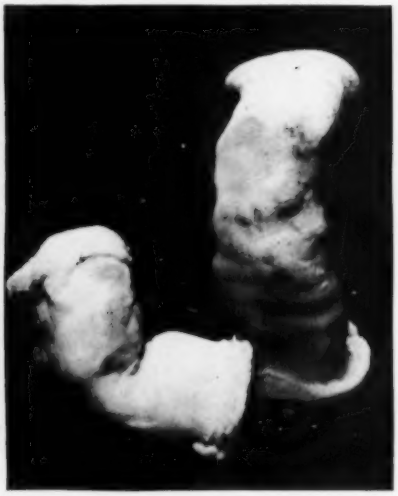

FIG. 10.—Photograph of two enterotomy sites in Dog No. 7. Treated with amniotic fluid. This animal had one adhesion to the incisional wound.

there were no adhesions about the site of enterotomy. In no case, however, was there imperfect healing of the intestine showing that the fluid had no obsorptive action on the 000 chromic catgut used for the intestinal suture.

TABLE VI—7 DOGS

Intestinal surgery

	Number of Dogs	Number of Adhesions	Filmy Adhesions	Firm Adhesions	Mortality
Control	2	0	2	2	0
Amniotic fluid	5	2*	2	3	0

* Intestines free of adhesions, but one adhesion between omentum and incision.
Note.—Some of the dogs showed both filmy and firm adhesions.

In view of the conclusions drawn by Johnson[2] and Warren[3] regarding the effect of the amniotic fluid on the cellular elements appearing in the process of repair after trauma to the peritoneum, smears were made of peritoneal fluids and traumatized serous surfaces. In the fourth group in which chemical peritonitis was produced by iodine (2 per cent.) smears were taken of the peritoneal fluid in the controls at twenty-four hours and in the animals treated with amniotic fluid at twenty-four and 120 hours. Both the control and treated animals at twenty-four hours showed brown particles within large macrophages. This we interpreted as iodine phagocytosed by mobilized histiocytes and leucocytes. There seemed to be a slight increase of polymorphonuclear leucocytes and many large free macrophages in the treated animals as compared with the control animals. This probably indicates a more vigorous defense reaction to local injury. A smear taken from the peritoneal fluid of a treated animal which had recovered from the peritonitis and was subsequently killed after 120 hours showed a preponderance of mobilized histiocytes and a very few fibroblasts. (Fig. 14.)

FIG. 11.—Photograph of loops of gut matted together with adhesions. Rat No. 12, first group. Treated with amniotic fluid.

Smears were taken from the fifth group twenty-four, seventy-two and 120 hours after operation. The peritoneal fluid of the control of twenty-four hours showed many red blood cells and a few macrophages and leucocytes. A smear from the treated animal at the same time showed a great reduction in the number of red cells and an increase in the number of macrophages, the predominating cell being cells of the polyblast type.

Smears from the sites of trauma in both control and treated animals showed many red blood cells. At seventy-two hours, the smears of the controls showed a preponderance of red blood cells while in the treated

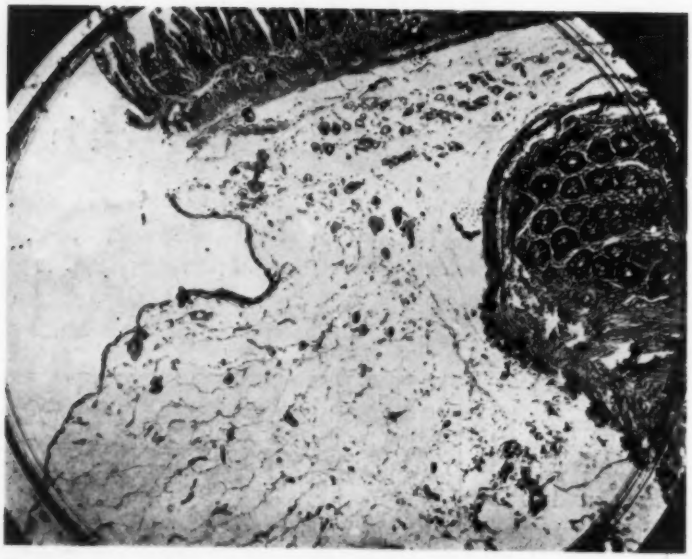

FIG. 12.—Microphotograph of a section of intestine shown in Fig. 11, showing the adhesions. Rat treated with amniotic fluid.

FIG. 13.—Photograph showing the matting together of intestines by adhesions. Rat No. 16 of first group. Treated with amniotic fluid.

FIG. 14.—Microphotograph of smear of peritoneal exudate from a rat which had survived a chemical peritonitis for one hundred and twenty hours. Treated with amniotic fluid.

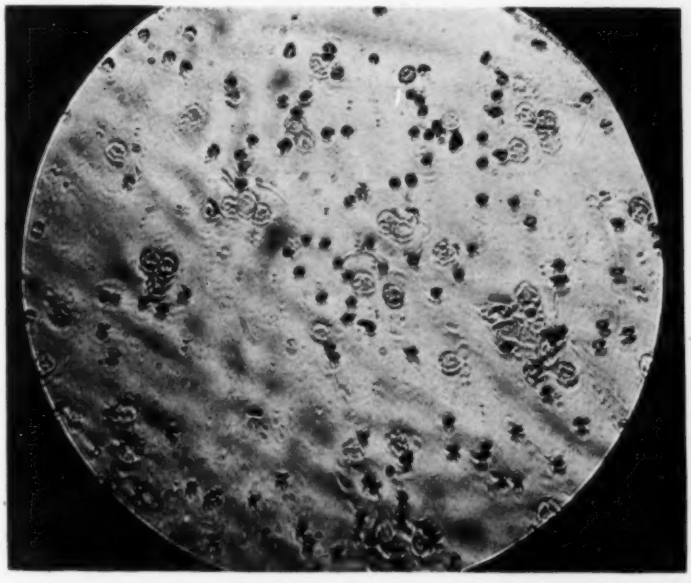

FIG. 15.—Microphotograph of a peritoneal from a rat twenty-four hours after peritoneal trauma. No amniotic fluid used. Note the relatively larger number of red-blood cells.

animals the proportion of red cells and polyblasts was about equal. Smears from the site of trauma at this time were nearly identical with the peritoneal fluid. There was practically no difference in the smears of the peritoneal fluid of the control and treated animals at 120 hours. Both showed a preponderance of the macrophages over the red blood cells. The smear from the side of trauma in the treated animal at 120 hours showed the first and only evidence of fibrin. No smears were made after 120 hours.

SUMMARY

The results of this investigation are not in accord with those reported previously. In only two of twenty-six treated animals which survived for a sufficient period was a complete absence of peritoneal adhesions observed. The extent of trauma which was produced may have been more severe than that previously used. It was our object to put amniotic fluid to a severe test since it is in cases with extensive trauma that it will have its greatest field of usefulness, if it is found to be a valuable adjunct in preventing adhesions.

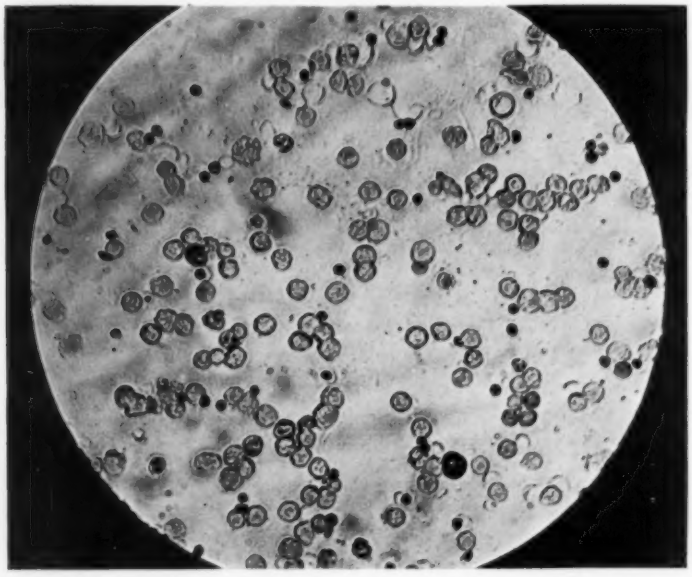

FIG. 16.—Microphotograph of a peritoneal smear from a rat twenty-four hours after peritoneal trauma. Treated with amniotic fluid. Note relatively small number of red-blood cells.

We have found the dividing line between filmy and firm adhesions difficult. Individual workers in the laboratory have varied somewhat in their classification of the specimens, but the figures remain relatively the same.

In the rats in which a chemical peritonitis was produced, the mortality of the treated group was less than that of the control group. The dilution of the iodine with amniotic fluid, however, must be considered as a factor in the reduction of mortality. Whether a diluted iodine solution in which

amniotic fluid was not used for dilution would give similar results must be determined.

TABLE VII—AUTOPSIED ANIMALS

Adhesions to incision—complete series—dogs and rats

	Number of Animals	Number of Adhesions	Per Cent.	Adhesions	Per Cent.
Control	16	10	62	6	37
Amniotic fluid	26	13	50	13	50

Smears taken from the peritoneum at twenty-four, seventy-two and 120 hours after trauma showed a reduction in the number of red blood cells and an increase in the macrophages, especially of the polyblast type, in the treated animals. This might be taken as confirmatory of Johnson's and Warren's observations concerning the action of amniotic fluid.

It would appear that amniotic fluid has no undesirable effect on a catgut suture line and that it does not prevent the formation of protective adhesions. In the dogs adhesions were less prominent in those in which amniotic fluid was used than in the controls.

Conclusions.—1. Amniotic fluid is apparently harmless when introduced into the peritoneal cavity.

2. It would seem to lessen the ooze from denuded surfaces and stimulate the peritoneum to a more powerful defense reaction.

3. It cannot be depended upon to prevent adhesions, although it possibly does modify the density of these.

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PATHOLOGICAL STUDY OF POSTERIOR VESICAL NECK OBSTRUCTION*

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Although the point of origin of posterior vesical neck obstruction has been subjected to intensive study by a few observers for many years, there are some conflicting theories about the origin. There are those who feel that the obstruction is due to a hypertrophy of true prostatic tissue, while others feel it may be due to hypertrophy of either the subcervical glands or the posterior commissural glands. They are all agreed on the inflammatory and

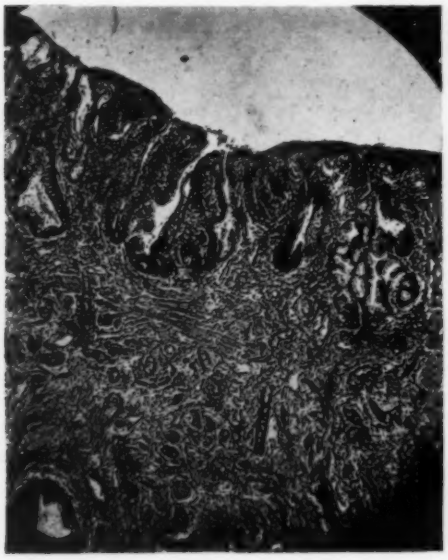

Fig. 1.—Microphotograph of normal tissues in region of posterior vesical neck, showing surface epithelium, subcervical glands, muscle tissue and one acinus of the posterior commissural glands.

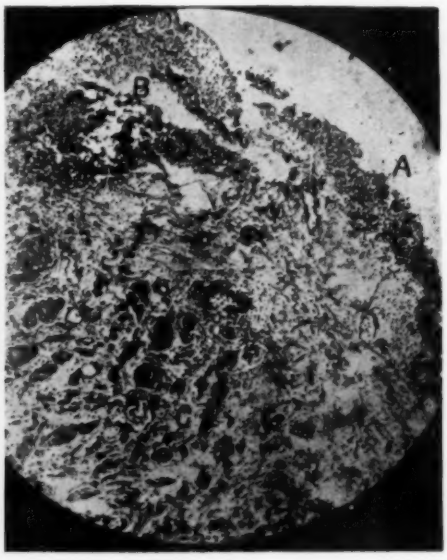

Fig. 2.—Microphotograph of inflammatory tissue obstructing posterior vesical neck. A—Transitional epithelium. B—Round-cell infiltration. C—Remaining muscle bundles.

congenital types. Randall,[1] in a study of gross specimens, concluded that in cases of median bar hypertrophy, the obstruction may be the result of a hypertrophy of either the subcervical glands of Albarran or a hypertrophy of the posterior commissural glands or a hypertrophy of both groups of glands.

This paper comprises: first, a brief review of the histological appearance of the normal posterior vesical neck; second, a résumé of the pre-operative genito-urinary findings; third, the pathological findings in fifty cases with

* Read before the Philadelphia Academy of Surgery, March 3, 1930.

posterior vesical neck obstruction; and, finally, a discussion of the different types.

Anatomically, there are two different glandular groups situated at the vesical neck in the mid-line, posteriorly; first, the subcervical glands of Albarran; and, secondly, the posterior commissural glands of true prostatic tissue. Examination of a histological section made in this region from normal tissue shows the subcervical glands situated in a loose supporting tissue under the transitional epithelium. The posterior commissural glands are under the subcervical glands but separated from them by a thick layer of muscle tissue. (Fig. 1.) This muscle tissue is part of the trigonal muscle which will be referred to later.

Symptomatology.—The symptoms in cases of posterior vesical neck obstruction are similar to those due to prostatic hypertrophy. A list of the genito-urinary symptoms and the number of patients having these symptoms in this series is given in Table I. When the disease was of long duration, many of the patients gave evidence of general health impairment from the frequent and urgent desire to urinate and from difficulty and straining on urination.

TABLE I

Symptoms

Frequency	50	Difficult urination	7
Nocturia	50	Pains in penis	6
Burning on urination	15	Incontinence	4
Urgency	12	Retention complete	3
Painful bladder	8	Retention intermittent	3
Dribbling	8	Impotence	2
Hematuria	1		

The duration of the disease in this series of cases is given in Table II.

TABLE II

Duration of Disease

5 weeks	1	5 years	6
4 months	4	6 years	3
6 months to 1 year	12	10 years	7
1 to 2 years	6	17 years	1
2 to 3 years	10		

The cystoscopic examination, in addition to showing definite posterior vesical neck elevation, frequently showed variant degrees of lateral lobe enlargement. There were but nine cases in which there was no change in the lateral vesical neck appearance. Trabeculation of the bladder was frequently seen, especially in those cases in which the duration of the disease was over a long period of time.

After removal of the posterior vesical neck obstruction, the lateral lobe enlargement soon subsided. This would indicate that the lateral bulging was due to œdema from the posterior vesical neck obstruction, rather than actual hypertrophy.

The cystoscopic appearance of the vesical neck is tabulated in Table III.

TABLE III

Vesical Neck Appearance

1. Median bar enlargement	9 cases
2. Median and lateral enlargement	38 cases
3. No record	3 cases

The accompanying Table IV shows the ages of the patients in this series.

TABLE IV

Ages

20 to 30	1	50 to 60	11
30 to 40	1	60 to 70	16
40 to 50	8	70 to 80	14

A review of the histological sections made from fifty cases with posterior vesical neck obstruction presents tissue variations which can be divided into four different groups.

The first group of sections consists of atrophic, sclerotic and granulation tissue with no evidence of hypertrophied tissues. (Fig. 2.) The second

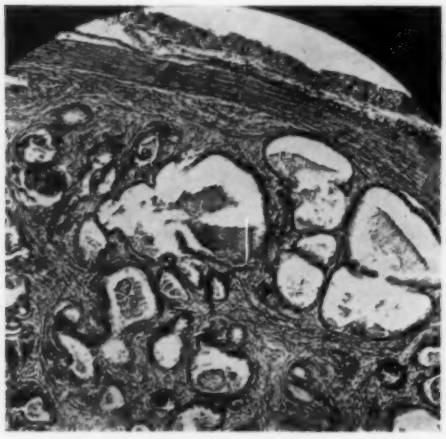

FIG. 3.—Microphotograph showing hypertrophied subcervical glands under the transitional epithelium.

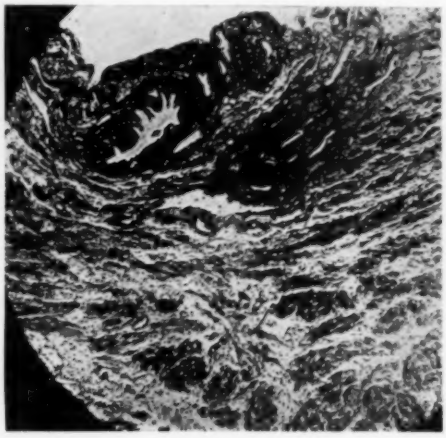

FIG. 4.—Microphotograph of hypertrophied muscle tissue obstructing the posterior vesical neck.

group consists of hypertrophied glandular tissue which is made up of varying sized acini scattered in a loose supporting tissue. The acini are lined with cuboidal and low columnar epithelium with some degree of intra-acinar papillary proliferation of these cells. (Fig. 3.) The third group consists entirely of muscle tissue, with no evidence of glandular hypertrophy. (Fig. 4.) Finally, the fourth group is made up of hypertrophied muscle tissue penetrated from below by hypertrophied glandular tissue. The glandular acini in this group appear similar to those in Group 2. (Fig. 5.)

Discussion.—While there is a definite difference in the histological findings in all four groups, the findings in Group 1 are undoubtedly the result of infection. The difference in Groups 2, 3, and 4 is apparently explainable on an anatomical basis.

Before discussing the latter groups, it is essential to review the relation of the trigonal muscle to the internal sphincter of the bladder as described by Young.[2] He frequently observed that during cystoscopy, if a violent desire to urinate came on, the trigone would contract greatly and the prostatic orifice would open widely, the posterior portion being apparently drawn backward by the muscle fibres which run from the trigone down into the posterior urethra and which were seen to contract violently. He feels that the opening of the internal sphincter during urination will have to be viewed as the result of the contraction of the powerful trigonal muscle which passes in the form of an arc through a weaker muscle of circular shape and pulls it down when it contracts. (Fig. 6.)

If one accepts this explanation of Young's, it will undoubtedly become apparent that hypertrophy of posterior commissural tissue would impair the action of the trigonal muscle. If this glandular tissue is sufficiently hyper-

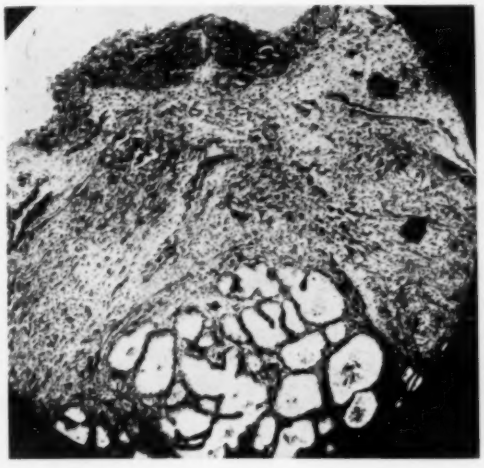

FIG. 5.—Microphotograph of hypertrophied muscle tissue penetrated by hypertrophied posterior commissural glands.

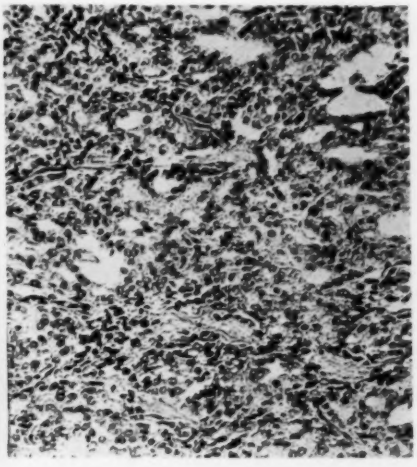

FIG. 7.—Microphotograph of adeno carcinoma of subcervical gland origin.

trophied over a long enough period of time, the trigonal muscle will have to put forth greater effort to push against this mass. The result of this increased effort on the part of the muscle causes it to hypertrophy. This muscle hypertrophy eventually becomes so great that it is the actual obstructing factor rather than the hypertrophied commissural tissue.

The foregoing evidence of Young's, given in connection with the microscopical findings in this series of cases, indicates that the hypertrophied muscle tissue seen in Group 3 is the result of overworked muscle on account of hypertrophied posterior commissural tissue.

From the histological findings in Group 4, it seems that the commissural glands in some cases hypertrophy to the degree of penetration through the hypertrophied trigonal muscle. If a patient with this type of tissue findings had presented himself for earlier treatment, the tissues removed would undoubtedly have been classified under Group 3.

The second group presents an entirely different histological picture. There is no evidence of hypertrophied muscle and the glandular tissue is situated under the transitional epithelium. We know that in the normal posterior neck, Albarran glands are in the subcutaneous tissue, and above the trigonal muscle. If these glands hypertrophy they grow out in the subcutaneous tissue, and on account of their location, have no effect upon the action of the trigonal muscle. Since in this group the later findings are evident, it is apparent that they illustrate obstruction from hypertrophy of the Albarran or subcervical group of glands.

In this series of cases studied there were three in which the obstructing tissues were adeno-carcinoma. Since there are two glandular groups at the vesical neck which may undergo benign hypertrophy, it is natural to assume that either of these groups may undergo carcinomatous changes. The lawless, penetrating manner in which malignancy grows makes it difficult in most cases to be sure of the point of origin. There was but one case in

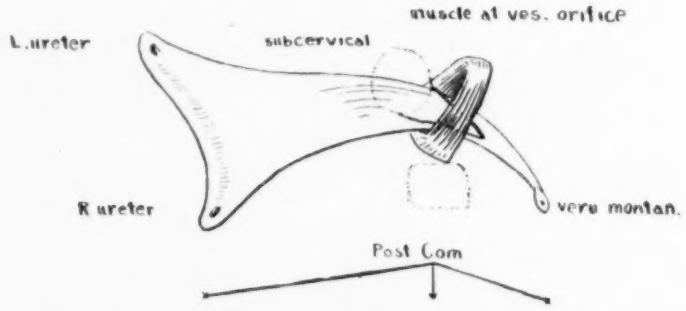

FIG. 6.—Modification of Young's diagram illustrating the relation of hypertrophied subcervical glands, and posterior commissural glands to the trigonal muscle.

which the carcinoma was found growing under the transitional epithelium with a histological appearance unlike those commonly seen in true prostatic glandular carcinoma. In this case the obstructing tissue was made up almost entirely of epithelial cells. These were very irregular in form and arrangement. There was very little stroma. The location and difference in appearance from the usual form of adeno-carcinoma of the prostatic glands would make one feel that it illustrates carcinomatous changes in subcervical glands. (Fig. 7.)

The following Table V, shows the pathological findings in this series of cases.

TABLE V

Pathological Findings

1. Inflammatory obstruction	2 cases
2. Hypertrophied muscle	26 cases
3. Hypertrophied muscle and gland	4 cases
4. Hypertrophied gland (*no* muscle hypertrophy)	15 cases
5. Adeno-carcinoma	3 cases

Conclusions.—This series of fifty cases of posterior vesical neck obstruction shows, first, that the symptomatology is similar to the symptomatology in diffuse prostatic hypertrophy; second, that the obstruction may be due to either inflammatory tissue, hypertrophy of subcervical glands or posterior commissural glands; and, finally, the subcervical glands as well as the posterior commissural glands may undergo carcinomatous change.

I am indebted to Dr. Alexander Randall for permission to include many of his cases in this study.

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TRANSACTIONS

OF THE

PHILADELPHIA ACADEMY OF SURGERY

STATED MEETING HELD MARCH 3RD, 1930

The President, DR. GEORGE P. MULLER, in the Chair

CALVIN M. SMYTH, JR., M.D., Recorder

OSTEOPERIOSTEAL BONE GRAFTS

DR. GEORGE M. DORRANCE read a paper with the above title for which see page 161.

DR. GEORGE WAGONER said that, since 1926, when he and Doctor Dorrance had done similar experimental work, he has had occasion to use the osteoperiosteal bone graft clinically. Several of his cases resulted in partial failure. The failures were due to the faulty preparation of the graft, there being areas in which bone chips were not adherent to the periostem. This was invariably found to be the case at time of re-operation, and, in Doctor Wagoner's opinion, explains the failures.

DR. ROBERT IVY said that his experience with bone grafts has been solely with the lower jaw and he has used the osteoperiosteal method and also the thick graft from the crest of the ilium. He feels that the osteoperiosteal graft is more useful in small defects on account of its simplicity. In a fairly long gap of two or three inches, the iliac graft is preferred, chiefly because it fills out the external deformity more satisfactorily. He agrees with Doctor Dorrance about the importance of fixation and immobilization in these cases.

DR. ASTLEY P. C. ASHHURST said that he thought that the first patient would have had a far better result with an ordinary excision of the knee-joint. He would have obtained his result in about eight weeks, although it would have been necessary to wear a brace for some time longer. The shortening accompanying this operation of excision is also an advantage, if the patient is to walk with a stiff knee, as it allows the heel to clear the ground in walking. In certain other locations, as in the shoulder, where the articular surfaces are smaller, the osteoperiosteal graft or some other extra-articular method of fixation should prove very valuable.

DR. GEORGE M. DORRANCE rejoined that he usually used excision, but that this man already had a short leg, and he wished also to avoid entering the joint and lighting up the old infection. He was sure that he has had better results with osteoperiosteal grafts than with full thickness grafts. It is a very simple operation, whereas putting a full thickness of graft in under the jaw is a formidable procedure. The last patient he operated upon

had had all the teeth removed, and it was a very simple procedure. That is what he is trying to bring out. The one patient shown surely proves that osteoperiosteal in the knees can be done.

WELCH BACILLUS ANTITOXIN IN INTESTINAL OBSTRUCTION

Dr. John P. North (by invitation) read a paper entitled, "The Use of Welch Bacillus Antitoxin in Intestinal Obstruction," for which see page 277.

Dr. Eldredge L. Eliason said about one year ago Doctor North and he investigated the mortality of acute intestinal obstruction in three hospitals. There was found to be the same as the average reported mortality of the country, approximately 30 per cent. There is a statement to the effect that in this country the mortality is actually nearly 60 per cent. C. Jeff Miller last year reported 343 cases taken from three hospitals in the South. He makes a statement that the mortality was between 60 and 65 per cent. rather than 35 and 40 per cent. This shows that there is still a very high mortality despite the fact that it is generally accepted today that dehydration and loss of chlorides on the one hand and toxemia on the other are the important factors. Replacement of chlorides by the administration of hypertonic salt solution and the relief of dehydration by large quantities of glucose have been extensively practiced for the last few years. The toxemia is another question. Much experimental work has been done and when William's report came they thought to attempt to confirm it. Doctor North had been unable to do this. It may be that the toxemia in dogs and human beings is not quite the same. Certain workers claim that dehydration and loss of chlorides in their dogs were responsible for their death and that they could find no evidence showing that toxemia had anything to do with it. So far, it has been impossible to attribute the cause of death in intestinal obstruction to any single factor and doubtless there is still much to be learned before definite conclusions can be drawn.

THE CONTRACTILE FUNCTION OF THE GALL-BLADDER

Dr. Isador S. Ravdin read a paper with the above title.

Dr. John H. Jopson remarked that this paper might better be discussed by a surgical physiologist rather than a clinical surgeon. The view that nothing which enters the gall-bladder through the cystic duct comes out by that route has been abandoned by practically all of its former advocates with the exception of Sweet and Halpert. They, apparently, have been left to hold the fort alone. From a purely philosophical standpoint, it seems incredible that nature would tolerate such an imperfect and complicated mechanism, designed for complete absorption of all bile entering it. Murphy and Higgins have demonstrated that, in animals in which experimental cholecystitis had been produced, the contractile function of the gall-bladder is restored when the cholecystitis clears up. Röntgenographic studies made after recovery showed normal behavior of the gall-bladder after the fat meal.

PERITONEAL ADHESIONS

Dr. James T. Lacey (by invitation) read a paper entitled, "The Use of Amniotic Fluid in the Prevention of Peritoneal Adhesions," for which see page 281.

Dr. Damon B. Pfeiffer said that he agreed with the proposition that when two peritoneal surfaces were brought in contact with each other and the endothelium survived, the adhesion was temporary, but if granulating surfaces were allowed to come in contact with each other the adhesions formed were permanent. In spite of the great variety of substances which have been used for the prevention of adhesions, nothing has changed their picture.

INTRAPERITONEAL PRESSURE

Dr. Richard H. Overhold (by invitation) read a paper entitled, "Observations on Intraperitoneal Pressure."

VESICAL NECK OBSTRUCTION

Dr. Albert E. Bothe read a paper entitled, "Pathological Study of Posterior Vesical Neck Obstruction," for which see page 300.

STATED MEETING HELD APRIL 7, 1930

RECONSTRUCTION OF AN ARM IN BRACHIAL PLEXUS INJURY

Dr. Benjamin F. Buzby reported the case of a man, aged forty-four, who, while at work on December 19, 1928, was struck by a falling plank and knocked down and then fell fifteen feet. He was admitted at once to the General Surgical Service of Cooper Hospital, Camden, N. J., wildly delirious. When admitted there was evident a laceration, four inches long, extending upward from the right eye-brow and a fracture of the right acromion shown by X-ray to be one of a simple transverse type. He had a marked concussion of the brain but an X-ray of his skull was negative. His scalp wound was cleansed surgically under an anæsthetic, his skull was inspected and no fracture discovered and the wound was sutured loosely and rubber tissue drainage inserted.

His previous medical history was negative.

Two days after admission he became rational and complained of numbness in his right upper extremity but as this was dressed at his side at the time for his fractured acromion no great attention was paid to it. Throughout the day a severe cellulitis of his face, neck and scalp became apparent, with a temperature range of 100.6° F. to 103° F. His scalp wound was opened at once and December 24, 1928, counterdrainage was established. The scalp was further drained on January 4, 1929, and again on January 24, 1929. During this period the man was very sick. His scalp wounds were entirely covered with dry crusts on February 6, 1929.

When the dressings were removed from his shoulder January 28, 1929, it was found that the man had no useful function in his right upper extremity. A neurological consultant at this time gave the opinion that the man had suffered damage to his cervical nerve root.

He was discharged from the hospital to the Out-Patient Neurological Service February 9, 1929, where he was found to have reactions of

degeneration in many muscles of his right arm. He was treated in the Physiotherapy Department by galvanism and massage. An X-ray of his cervical spine April 2, 1929, showed a crushed fracture of the body of the sixth cervical vertebra with an old fracture of the fifth cervical spinous process.

He was referred to the Orthopædic Service for reconstruction of his arm, if possible, on June 4, 1929. It was found at this time that the man had complete and total paralysis with advanced atrophy of all muscles supplied by the fifth and sixth cervical roots of the brachial plexus, *e.g.*, supra and infraspinatus, subscapularis, teres major and minor, levator anguli scapulæ, rhomboideus major and minor, deltoid, biceps, brachialis anticus, brachioradialis, supinator brevis, pronator radii teres, flexor carpi radialis and palmaris longus.

The serratus magnus also was involved as evidenced by the winged scapula, showing that the damage had been done to the fifth and sixth roots close up to or in the vertebral foramina before the branches came off from these roots to help form, with a branch from the seventh cervical root, the long thoracic nerve.

The whole arm hung limp at the side with no power above the elbow except the triceps, and the humeral head was depressed at least one and one-quarter inch from the acromion. There was no power to externally or internally rotate the humerus except by means of the pectorals and latissimus dorsi. There was no power to abduct the shoulder, flex the elbow or supinate the forearm. Sensation was disturbed but not abolished anywhere. His neck motions were full and free. He had power to shrug his shoulder by means of the trapezius.

It was felt that since his injury to the brachial plexus was so centrally located, function for minor use was better than none at all, so accordingly, June 13, 1929, an arthrodesis of his right shoulder was done. The bones were found very soft and atrophic. After destroying the articulating surface of the humeral head, glenoid, and under surface of the acromion, the head was suspended and fastened to the acromion by an encircling suture of kangaroo tendon. The arm was put in plaster of Paris in 60° of abduction and 45° of external rotation and kept there until August 1, 1929, when the case was changed. The new one was kept on until September 17, 1929. His post-operative course was uneventful. When the case was finally removed his shoulder was in fair position and stiff but there was no bony union. He had power through the trapezius to actively abduct the arm 30°.

Even though he had no power in the supinator longus, the muscle usually used when transplanted up the humerus to act as a flexor of the elbow, it was felt that it was worth a trial to transplant the remaining extensor muscle group attached to the external humeral condyle higher up the humerus and thus make these muscles do double duty, as it were—elbow flexion and wrist extension. This was done October 9, 1929, by separating subperiosteally the muscle origins from the external condyle and fastening them subperiosteally one and one-half inch up the outer side of the humeral shaft by means of kangaroo tendon passed through drill holes in the shaft. The arm was then fixed in flexion 20° above a right angle in an internal angular plaster splint until December 6, 1929, but massage and guided active motion were begun November 1, 1929. When his splint was finally removed, the active motion of his elbow was from 100° to 60° and he could actively abduct his shoulder 70° from his side even though the shoulder arthrodesis did not show bony union.

At present he is able to fully flex his elbow with his shoulder abducted and easily gets his hand to his mouth. In so doing the flexors of his wrist must contract against the pull of the extensors to fix the wrist so that the extensor insertions may act as origins. By so doing his hand goes into radial deviation of 20°.

As measured now his active movements are: abduction of the whole shoulder girdle, 60°; flexion of elbow to 40°; extension of elbow to 160°; and external rotation 25°.

The patient is anxious to get more external rotation of the shoulder so it is proposed soon to try and give him complete bony ankylosis of his shoulder in a more advantageous amount of external rotation.

Neurological surgeons may say that suture of the divided roots should have been attempted first, since no serious irreparable damage has been done to the muscles supplied by the torn fifth and sixth cervical roots that still could be done, if feasible, and the man's permanent disability would be then only the fibrous ankylosis of the shoulder, which exists often enough as the result of disease or injury in patients now leading active, useful lives.

TRAUMATIC BRACHIAL PLEXUS PARALYSIS

Dr. Thomas Shallow read a paper with the above title for which see page 182.

THE CAUSE AND ELIMINATION OF REACTIONS AFTER INTRAVENOUS INFUSIONS

Dr. Lee A. Rademaker read, by invitation, a paper with the above title for which see page 195.

GASTRIC ULCER

Dr. Edward Watts Saunders, of New York City, read, by invitation, a paper entitled, "A Bacteriological and Clinical Study of Gastric Ulcer," for which see page 222.

Dr. J. Edwin Sweet, of New York City, said that Doctor Saunders did not start this work with the view of finding the cause of peptic ulcer. Sometimes it is most useful to try to solve some peculiar feature of a problem, rather than to tackle the whole thing. Doctor Saunders started from two clinical facts; ulcer is a human disease, it is a chronic disease. Just at that time Doctor Lambert and Doctor Weeks were working in the laboratory on the problem of lung abscess—another human disease, another chronic disease. They were able to show in sections a ring of spirochetes advancing into the lung tissue ahead of the pus producers, apparently the reason for their chronicity. So Doctor Saunders tried the same technic—Levadity staining of properly fixed material from ulcers. He did not find spirochetes, but did find what seemed to be longer and shorter chains of streptococci.

He was then particularly fortunate in having the advice of Doctor Torrey and Doctor Kahn, of the Department of Public Health, who suggested Humtoon's medium or hormone agar. The results of this work he has shown in this paper. Especially noteworthy is the fact that of nineteen cultural attempts, ten showed the same organism in pure culture; four more showed the addition of a yeast; the rest, different casual contaminations. One would

have expected to find the entire flora of the mouth in an ulcer of the stomach.

Doctor Saunders finds no relationship between these organisms and the organisms of the so-called foci of infection; the theory of the focus of infection in ulcer is very persistent even though it would not appear from the literature that the pursuit of this theory has led to any very remarkable clinical results.

Doctor Saunders, being a surgeon, would have been justified in throwing up his hands in holy horror when he found his work heading into the abstruse problem of modern bacteriology—mutation. It seems that herein may lie an explanation for the most remarkable facts concerning ulcer; the relation of ulcer to body type; the seasonal occurrence, or recurrence; the strict limitation to the pyloric area; the explanation of the results of surgery.

Perhaps all believe in the hydrochloric theory of ulcer. It has, however, never satisfied the speaker; the ejected stream, impinging on the duodenal wall sounds good for the post-pyloric location, but does not seem to explain the pre-pyloric location. Nor has anyone offered any evidence that more acid squirts harder in November than in July.

It seems a far more likely hypothesis, and one in closer conformity to the facts, to assume that the disturbance is of the regurgitation of bile, and the effects of bile or some contained factor in the bile, upon the growth and virulence of the organism.

If Doctor Saunders' findings are accepted, it must be assumed that this organism grows only in a medium of the right degree of acidity; therefore, in the body it can grow only in the skin, the mouth, the stomach, and in the stomach it finds the correct pH around the pylorus. But a further factor is needed to explain the seasonal peculiarity of ulcer and its adherence to the asthenic type. A working hypothesis is that this second factor is the bile and perhaps some particular factor in the bile which reacts to seasonal influences.

Possibly the situation is this: in the asthenic type the duodenum is so kinked that bile, with or without this supposititious second factor, does not get to the pyloric region at all.

Rest in bed cures by relieving this kink. Gastroenterostomy cures by permitting access of bile into the stomach, whence it flows out, through the pylorus, over the ulcer. The only sterile cultures in Doctor Saunders' work have been in cases in which a gastroenterostomy was present. Resection cures by removing that area where this organism can grow; it savors somewhat of the method of curing a bunion by amputation through the mid-thigh—doubtless effective, but somewhat strenuous. Pyloroplasty does not help because the bile factor misses the ulcer area entirely.

Ulcers do occur in the plethoric type but how often does this happen without concomitant gall-bladder disease? If the biliary tract is diseased, then this supposititious factor in the bile may be lacking.

CHRONIC ARTHRITIS SHOWING IMPROVEMENT FOLLOWING LUMBAR SYMPATHECTOMY

Dr. Charles H. Frazier remarked that there are certain forms of arthritis, call them what you will, rheumatoid arthritis or arthritis deformans in which the patients often suffer from cold, clammy hands and feet. There are areas of pallor and cyanosis of the extremities, the tissues are puffy and often the surface is covered with a film of moisture. One might with propriety interpret these as signs of vasoconstriction; certainly there is a vascular disturbance involving the arterioles and capillaries. It is well known that there are certain forms of arthritis that are of neurogenic origin, as, for example, in Charcot's disease and syringomyelia.

Surgeons have been in the habit of speaking of these chronic forms of arthritis mostly from the infective point of view. The question now comes up, especially in view of the observations which have been made following gangliectomy, whether some of these forms of arthritis may not be due to imperfect nutrition, as the result of vasospasm.

So far as the speaker knows, the first observation as to the effect of sympathectomy was made by Rowntree and Adson (*Transactions Assoc. Amer. Physicians*, vol. xi: v, p. 221, 1929), and the results of their operation were so striking that Doctor Frazier ventured to apply this treatment to a case which was brought to his attention from the Medical Service of the University Hospital.

As a result of this observation Rowntree and Adson state that in certain types of arthritis the sympathetic nervous system of the extremities is hyperactive, producing marked vasomotor disturbance and profuse sweating, possibly contributing to the spasm and atrophy of the muscles with the resultant deformity. The clinical picture is characterized by coldness of the extremities, marked sweating, trophic changes of the muscles, skin and nails, tender, painful, and swollen joints. All these abnormal manifestations disappeared on release of the extremities from sympathetic control.

Certainly in times past we have been in the habit of expecting temporary relief at least from such measures as might increase the circulation and temperature of the joint, more particularly hot applications, physiotherapy, baking, diathemy.

Report of a Case.—W. P., aged twenty-five years (File No. 17921), was referred to the Neurosurgical Service of the University Hospital from the Medical Department October 29, 1929.

History.—The first attack of joint pain and swelling was in 1923, lasting three months and affecting many joints. A second attack occurred in February, 1926, which lasted until May, 1926, and a third attack began in December, 1926, the latter, however, of less severity than the two previous attacks.

May 18, 1927, to June 26, 1927, the patient was studied on the Medical Service of the University Hospital with the following findings: small buried tonsils; congenital deformity of right hand and chest; evidence of arthritis in right wrist, right elbow and both ankles. X-ray showed abscess of upper molar tooth, left wrist and ankles showed orthopædic changes.

Treatment.—Tonsillectomy and extraction of teeth.

Readmitted October 16, 1929. In the interim patient has had several similar attacks. In September, 1929, the bottom of his right foot became painful and slightly swollen, great toes of both feet began to swell and cause pain; the joints were neither hot or reddened in this attack. Pain next appeared in sacroiliac region.

Operations.—December 28, 1929: Left lumbar ganglionectomy L. 2, 3 and 4; January 2, 1930: paravertebral injection of the thoracic ganglion; January 27, 1930: right lumbar ganglionectomy, L. 2, 3 and 4.

The effect of the operations has been more than gratifying. The freedom with which the patient moves now is very much greater than before. Of course, certain structural changes had already prevented perfect freedom of motion in his knee-joints but those who observed him before the operation and afterwards, called attention especially to the greater freedom with which he walks, the erect station of the trunk which heretofore had been bent forward.

This case, Doctor Frazier thought, was an excellent one for demonstration because the process in the left upper extremity, especially the wrist-joint, had already reached the terminal stage; that is, there was complete ankylosis of the wrist-joint. The process in the lower extremities, as in the knees and ankles, was not nearly so far advanced so that here we have an opportunity to demonstrate whether or not the sympathectomy may arrest the process, whatever it may be, in these forms of chronic arthritis.

TRANSACTIONS
OF THE
NEW YORK SURGICAL SOCIETY

STATED MEETING HELD APRIL 9, 1930

The Vice-President, Dr. John Douglas, in the Chair

CONSECUTIVE PERFORATIONS OF STOMACH AND OF DUODENUM

Dr. William F. Cunningham presented a man who, when thirty-six years of age, was admitted to the First Surgical Division of Bellevue Hospital, April 16, 1929. Seven and one-half hours prior to admission he suddenly developed a sharp pain in the epigastrium, which gradually spread over the entire abdomen. He vomited once a short time before admission. The abdomen presented signs of generalized peritoneal irritation. Temperature 101, pulse 90, white blood cells 15,000 with 91 per cent. polymorphonuclears. Urine contained a very faint trace of albumin. The man had suffered indefinite gastric symptoms for three weeks previously and had indulged freely in alcohol for relief. An immediate operation was performed and a perforation three millimetres in diameter on the anterior wall of the stomach close to the antrum was found, actively emitting brownish fluid. It was surrounded by a wide, indurated area. The perforation was closed with two purse string sutures. A culture taken from the peritoneal fluid was reported as sterile. With the exception of an acute bronchitis he made an uneventful recovery and was discharged from the hospital seventeen days after operation.

Seven months later, November 18, 1929, he was readmitted about four hours after recurrence of sudden, severe, epigastric pain following one week of post-prandial discomfort and constipation. The pain had spread over the entire right abdomen, which, on admission, again presented the signs of generalized peritoneal irritation. Temperature 100, pulse 100, white blood cells 10,200 with 88 per cent. polymorphonuclears. Urine negative.

At operation a four-millimetre perforation was found on the anterior wall of the first portion of the duodenum. At the time of operation it was sealed off by the liver. There was present a large amount of turbid, whitish fluid in the peritoneal cavity, the intestines were injected and fibrin was present. There was a large collection of fluid between the liver and the diaphragm. The perforation was closed by a purse string suture of chromic gut. There was no peritoneal evidence of the previous gastric perforation. Culture of peritoneal fluid showed B. Coli. Temperature rose to 103 within the first twenty-four hours and gradually subsided to normal on the fifth day.

December 11 (twenty-three days post-operative) a gastro-intestinal series was made and showed no evidence of any gastric or duodenal ulcer.

On February 4, 1930 (two and one-half months post-operative) he complained of occasional gas but has had no pain and has gained in weight. Fleuroscopic examination and films made at this time presented no evidence of duodenal ulcer.

This patient was presented because he offered a rather unusual occurrence of perforation of a gastric ulcer, followed seven months later by perforation of an acute duodenal ulcer and presents no X-ray evidence of duodenal abnormality twenty-three days post-operative. In a series of ninety-two per-

forated ulcers he had seen two other cases of recurrent perforation—one similar to the case presented—the other a recurrent duodenal perforation.

Dr. John Douglas said that it had often been his experience, in these cases of recurrent ulcers, to find there was present somewhere in the body a focus of infection, frequently carious teeth. Also, with carious teeth, they do not properly masticate food. Whether or not, however, this has anything to do with the etiology of duodenal or gastric ulcer, it is important in these cases to get the teeth cleaned, if possible before operation, or otherwise before they leave the hospital.

CARCINOMA OF RECTUM

Dr. W. F. Cunningham presented a woman, fifty-four years of age, who was admitted to the First Surgical Division of Bellevue Hospital January 8, 1927. For six months she had suffered from painful defecation with bleeding. The calibre of stools had been greatly reduced in size during this time. No history of diarrhœa, constipation or mucous discharge. She had lost weight but the amount, though considerable, was indefinite. For some months she had had pain along the course of the left sciatic nerve. Examination revealed, on the anterior rectal wall, beginning at level of sphincter and extending upward one and one-half inches and involving one-half the circumference of the rectum, an ulcerated area with indurated rolled edges. It was infiltrating the posterior vaginal wall. Biopsy showed this to be an adenocarcinoma.

January 17 a permanent sigmoid colostomy was made and forty-eight hours later this loop was opened by cautery.

January 29 the following procedure was performed. The tumor mass in the rectum invaded the posterior vaginal wall over an area six by two centimetres. Incisions were made in the vaginal wall postero-laterally, deepened and carried through so as to surround the rectum, circumscribing the perineal body, the sphincters and anus. The rectum was freed by sharp and blunt dissection with the posterior vaginal wall. The vaginal wall was then repaired and the rectum brought down for a distance of five inches and excised, the upper end being sutured to the skin margins. The wound was loosely packed with iodoform gauze. Post-operative reaction was slight but there was considerable free suppuration. The colostomy worked well. The patient was discharged from the hospital four weeks after operation. At the present time there is no evidence of local recurrence or remote metastasis. The post-vaginal wall is intact, the perineum is represented by a thin shred of skin, and rectal mucosa remains at the edge of the skin incision. While the operative procedure was intended as a palliation simplex, done to prevent extensive recto-vaginal ulceration and its associated unpleasantness, it has given an extremely satisfactory surgical result over a three-year period.

KNEE-JOINT ARTHROTOMY FOR HYPERTROPHIC OSTEOARTHRITIS

Dr. John J. Moorhead presented a woman whose left knee had been a source of trouble for eighteen years, but had been an actual disabling feature for three years. Pain limitation of motion and repeated swelling of the joint had been the main symptoms. Various forms of internal treatment together with a course of vaccines proved unavailing. Physiotherapy likewise gave no lasting effects. Foci of infection have been diligently searched for.

She was first seen by the reporter November 17, 1927. At that time the left knee was in a flexed position, fifteen degrees off a straight line, and

could not be straightened therefrom. Flexion was limited to a right angle. There was considerable atrophy of the calf and thigh and there was a sharp tenderness over the external semilunar region. There was fibrous crepitation in the enlarged joint. No heat; X-rays negative.

February 16, 1928, at Post-Graduate Hospital, a medio-lateral arthrotomy was performed under strict Lane technic, a tourniquet being used. The findings were hypertrophic synovitis with an erosion of both semilunars and hypertrophy of the subpatellar fat pads. Both semilunars were excised together with a part of the subpatellar fat pads and the synovial lining. She made a very satisfactory recovery and two months later she estimated that she had a 75 per cent. improvement as to pain and function. In October, eight months after the operation, she stated that she had walked a distance of seven miles without limping. At the present time the knee-joint motion is practically complete and she has little if any pain. Here is a case of long-standing intra-articular involvement which twenty-six months after operation shows practically a perfect outcome.

He had had a number of similar cases and in all had performed 143 knee-joint arthrotomies by this same ultra-aseptic technic. Fifty-nine of these cases were reported before this Society in November, 1925. His conviction is that there are a large number of these knee-joint cases in which surgery is indicated. All, of course, realize that knee-joint calculi (damaged semilunars, exostoses or the like) are subjects for arthrotomy. There is, however, in addition, a large group in which arthritis with or without injury is the main factor and it is into that class that this case falls.

Dr. Clay Ray Murray queried the condition of the alar ligaments in this case. He had sometimes found evidence of crushing of these ligaments in similar cases, producing effusion and even locking the joint as they are pinched between tibia and femur. Was it possible that such a condition accounted for the symptoms in the case presented?

Doctor Moorhead added that in this case the patella was dislocated to the outer side and that no muscle fibres were cut inasmuch as the vastus internus was separated in much the same manner as the rectus in a laparotomy. After the lateral compartments had been exposed, the knee was bent and, if necessary, the incision was lengthened and thus, with rotation, the external semilunar could also be exposed. The Jones patella split operation had been abandoned some years ago because this medio-lateral incision gave just as good access without interfering with the knee pan. A smaller incision has also been abandoned because experience has shown that there is usually a combination of pathology in the joint even though the symptoms may point to one major process.

BILATERAL SUBCUTANEOUS RUPTURED QUADRICEPS

Dr. John J. Moorhead presented a woman who, on October 18, 1924, tripped on stairs and fell three steps. She was in bed ten days and subsequently needed a crutch and cane. She was first seen by the reporter September 15, 1926. Her right knee was painful, and, when flexed, could not be extended. There was considerable atrophy of the right thigh and leg. There was a distinct gap, three fingers wide, between the top of the patella

and the lower end of the quadriceps. There was evidence of hypertrophic arthritis around both knee-joints.

At operation at Post-Graduate Hospital, September 28, 1926, it was found that there had been a subcutaneous laceration of the quadriceps tendon close to its attachment and that there was evidence of calcification thereof. The edges were freshened and chromic sutures were applied and a posterior splint was attached. She recovered fairly well and had greater control of the extension. February 9, 1927, the knee gave way and she fell and thereafter there was considerable loss of function, so that March 14, 1927, she was re-operated upon and a double pedicle flap was fashioned by turning down the margins of the quadriceps tendon. Reinforcement was made by drilling holes through the patella. Since then she has regained only partial function in this right knee.

September 21, 1929, she fell and injured the left knee and on the twenty-third of September, the left quadriceps was sutured, reinforcement being made through holes drilled in the top of the patella. She has made a most satisfactory recovery as to the left knee.

This is a case in which several operations have been performed—on one side after a lapse of two years and on the opposite side after a lapse of two days; and the contrast in end results is apparent.

Dr. Robert H. Kennedy thought this case an excellent example of the result of early operation. He had occasion ten years ago to attend a man who had a bilateral rupture of the quadriceps extensor tendons about one-quarter inch above the patella, through an automobile accident. He was operated on four days later. The ruptured tendons and joint capsules were sutured in layers on both sides and the extremities immobilized for four weeks. He was a very stout man and for some years had felt that his knees were unstable in walking. He was last seen twenty months after operation when he felt that his legs were much more stable. At that time function of both lower extremities was complete and he had no complaints.

Dr. Clay Ray Murray emphasized the difficulties encountered in late operative treatment of these cases, both in identifying structures and pathology, and in securing full functional recovery. Failure to institute primary operative treatment is often due to too superficial examination and the ready diagnosis of traumatic synovitis. In a recently operated case of rupture of the patellar tendon of eleven months' duration with total loss of extension, this had been the diagnosis made at the time of the original injury, and the sole treatment had been rest and physio-therapy. At operation, eleven months after the injury, it was extremely difficult to spell out the pathology and identify in the scar tissue the site of the original tear in the tendon and in the lateral expansions. Any knee-joint which shows effusion into the joint very shortly after injury is a hemarthrosis and not a synovitis, and should be carefully examined for a lesion capable of producing a hemarthrosis.

Dr. Hugh Auchincloss referred to a man, about sixty-five years of age, whom he had cared for, who had sustained a complete fracture of the quadriceps tendon just above the patella incidental to taking an unexpected step down from the curb. The patella had remained intact. Repair was made by weaving a broad fascial strip cut from the tensor fasciæ femoris, starting

just below and encircling the patella, into the quadriceps muscle above. The repair seemed firm and the motion of the knee good. Several months later he was knocked down by a taxi-cab and run over, a rear wheel passing over the lower end of the same thigh. The driver braked suddenly and brought his car to a stop so that the wheel was resting practically on the site of the former injury when the patient shouted to him to move on so the leg could be freed. A large hematoma resulted, that had to be evacuated, but it is interesting to note that the repair of the ruptured quadriceps tendon was not affected. These cases are not so frequent that the technic for their repair has become standardized. This method, by means of the fascial suture, worked so well that it is perhaps worth while recording.

DEPRESSED FRACTURE OF CHEST WALL WITH HERNIA OF LUNG

Dr. John J. Moorhead presented a man who, May 22, 1929, fell through an elevator shaft, a distance of twenty to twenty-five feet, striking upper part of front of right chest against a projection. He was three weeks in a local hospital where the treatment was rest in bed and strapping of the chest wall for broken ribs. He was first seen by the reporter November 15, 1929. At that time he complained of a bulging in the right upper chest with pain and disability in the same location. He had not returned to work since the date of accident. This bulging and pain were increased on coughing or straining. On deep expiration a mass could be made to appear in the right upper chest. Examination at that time showed a visible and palpable ridge of bone on the inner side of the right nipple and this marked a cup-like depression in the neighborhood of the nipple approximately four inches by one and one-half inches in size. The musculature in this neighborhood was definitely flabby and atrophic and the general appearance was a sunken-in section of the chest wall. On moving or deep expiration a bulging in this hollowed-out area appeared in size equal to half a good-sized orange. It immediately disappeared at the end of expiration and apparently was a hernia of the lung.

December 7, 1929, at the Post-Graduate Hospital under gas-oxygen-ether anæsthesia, a semi-circular incision was made exposing this area and it was then found that the third, fourth and fifth ribs were markedly depressed and overlapping. In the centre of this depressed area a mass appeared at each act of expiration and when it had been dissected down to its base, it was found to represent a thick pleura which escaped from a gap between the broken ribs, the base of this hernia sac being about one and one-half inches in diameter. When it was opened there was an immediate collapse of the underlying lung. The base of the sac was transfixed and inverted after the manner of an ordinary hernia; the intercostal and pectoral muscles were plicated after the third rib had been elevated into a better position and a stab wound drain was inserted in the neighborhood of the axilla. In general the approach was similar to that made on the inner half of an excision of the breast.

He had a stormy convalescence and developed a post-operative pneumonia on the right side and a hematoma formed along attachments of his pectoralis major. This became infected and a secondary drainage opening was made. He was discharged from the hospital December 29, 1929. The wound is entirely closed now except for a small sinus which apparently leads down to the necrotic end of one of the fractured ribs.

There has been no recurrence of the hernia despite the apparent gap in the

bone cage of the chest. He has gained twenty-five pounds since leaving the hospital.

OSTEOMYELITIS OF TIBIA WITH SECONDARY BONE GRAFT

Dr. William Crawford White presented a boy, eight years of age, when admitted to Roosevelt Hospital on December 18, 1926, with a diagnosis of chronic suppurative osteomyelitis of left tibia, right humerus, and

Fig. 1.—When admitted to hospital.

Fig. 2.—After first operation.

right femur. He had been sick for eight weeks following a scratch on his left ankle with the edge of a roller skate. Two days afterward, this scratched abrasion became painful, swollen and red. The local condition was treated by his physician who incised and drained the abscess. Subsequently swelling in the right shoulder and right knee region developed. Both these areas were incised and drained. Culture showed staphylococcus aureus.

On December 31, 1926, he was operated upon by the speaker who then found extensive metaphysis involvement and it appeared that the whole bone

was destroyed. There was thick white pus in the medulla. A subperiosteal removal of the metaphysis was then performed with a Giglee saw. The bone was cut across just proximal to the distal epiphysis and just distal to the upper epithysis. The wound was partly packed with iodoform gauze but for the most part the periosteum was approximated with interrupted plain catgut. A posterior plaster splint was applied.

Leg suspension and traction was used for the left lower extremity. Bone regeneration was extremely slow in the left tibia. He remained in the hos-

FIG. 3.—Skiagram taken April 10, 1928, showing maximum periosteal growth.

FIG. 4.—Two months after bone grafting.

FIG. 5.—Present condition. Two years after bone grafting.

pital for six months and at the time of discharge there was no new bone at the lower portion of the wound. He was discharged to the dispensary on June 13, 1926.

He was seen from time to time in the Recall Clinic, and the condition appeared to remain the same. He was still walking on crutches and used a molded plaster splint. It was decided that a bone graft might help the condition. The leg wound was healed.

On April 13, 1928, about sixteen months after the first operation, a bone graft was taken from the right leg and inserted into the left leg. Bone had been well formed in the upper part of the left tibia but it narrowed down rapidly in a cone-shaped fashion until at the junction of the middle and lower third there was a space about three inches long with no bone, just a tube of periosteal tissue. (Fig. 3.) Beyond this, there was new bone formation in the diaphysis which was soft and crumbly. A longitudinal incision along the anterior inner surface of the left leg was made with exposure from the upper end of the bone to the lower end. Incision of periosteum which was stripped back. Along the inner side of this new bone in the middle third a strip of bone was removed. A slot was made in the lower end and also in the upper end of the new bone. This gave a length of eight inches to be filled with grafts. An eight-inch graft about five-eighths inch in width was removed with periosteum from the right tibia. This was placed in the slot prepared for it in the left leg and held in place by circular kangaroo tendon sutures. The wound was closed with drainage.

June 9, 1928, a plaster circular splint applied. On the fifty-seventh day the splint was removed and the wound was examined. There were three sinuses present; one at the upper end of the scar and two at the lower end, with some yellow pus. The leg was dressed and placed in a posterior wire splint. On June 26, 1928, he was discharged to the dispensary with a posterior splint on his seventy-fourth day. He was kept on crutches with a posterior splint.

In October, 1928, X-ray showed a complete osseous bridge. Subsequently there has been a slow but steady improvement and in June, 1929, he was allowed to walk without any support. On April 5, 1930, he was examined and found to have one and one-half inches of shortening of the left leg as compared to the right. He walks on his left toes to compensate. The wound is completely healed and there is good firm bone. There is complete motion at the left ankle-joint and left knee-joint. There is no rotation of the lower part of the leg on the upper part.

This boy was shown, not to demonstrate the value of subperiosteal resection for acute osteomyelitis, but to demonstrate regeneration of bone in an area that had been chronically infected, not one in which regeneration had recurred from the periosteum. Dr. James I. Russell has shown before this Society a number of similar subperiosteal resections with regeneration of bone, and this is the first case that had failed to regenerate.

Dr. Kirby Dwight said that an interesting thing about these bone grafts was that a small amount of infection did not vitiate the graft. Bone grafting is so frequently done in cases in which there has been long-standing infection that there are likely to be residual bacteria in the scar tissue and the best of them may become infected. One might be tempted to discouragement on seeing pus appear, seeping through the plaster cast, but this is a mistake. Union may take place even though a sinus has formed and persists for some time.

Dr. Frederic W. Bancroft remarked as to complete subperiosteal resection in cases of acute osteomyelitis that Nichols, a number of years ago, advised removal of the sequestrum after the involucrum had become one to two millimetres in thickness. This would mean at about six to eight weeks after the primary drainage of the medulla. He advised in these cases the

suture of the periosteum and the occlusion of the dead space, but it was at a time when new bone had already started to proliferate.

In a discussion held recently in Philadelphia, Doctor Pfeiffer, in a study of a series of cases, showed that the operative procedure which drained the metaphysis inflicting the minimum amount of trauma had produced the best results. It was generally felt that the stripping of the periosteum and curettage of the medullary canal were inadvisable, as they might cause further interference with the blood-supply of bone which had already received considerable damage by infection.

Doctor White, in closing the discussion, replied to Doctor Bancroft that this subperiosteal resection had not been done since 1926, but he felt that there were indications for the operation at times as this had been the only case in a series of five that had failed to reform bone. This case, however, was not shown to demonstrate a poor result from periosteal resection; rather, it was shown to demonstrate the formation of new bone in an infected area by the use of a bone graft with periosteum. Before the operation the limb was useless; now there is bone continuity with a useful limb.

RAT-BITE FEVER

Dr. William Crawford White presented a negro baby boy, aged eight months, who was admitted to the Surgical Service of Roosevelt Hospital June 7, 1929. He remained there three days when he was discharged. He was readmitted three days later and finally discharged at the end of seven weeks.

A high fever was noted on first admission. This came down by crises to normal on the following day. The history stated that three weeks before admission the child was bitten by a rat on the upper and lower lips. He was taken to another hospital where the wound was treated. About ten days later both lips began to swell. This was associated with some fever.

On admission to the Roosevelt Hospital the child appeared acutely ill with a fever of 104.6°. Both lips were swollen and indurated, while the sublingual, submaxillary, and cervical lymph nodes were enlarged. No rash was noted. At that time a diagnosis of cellulitis of the upper and lower lips with cervical adenitis was made. Wet dressings were applied, and after three days the child was sent home.

He returned three days later with a fever of 103.6°. By this time the swelling of the lips had almost disappeared, but the cervical lymph nodes were enlarged. The child appeared sick, and it was then that serological tests were made and blood cultures taken. Except for a moderate rachitic condition the examination was essentially negative. A sample of the patient's blood showed a few spirochætæ by means of the dark field illumination. A rare one was found by means of an unstained smear. The organisms were morphologically identical with spirochætæ morsus muris. Three mice and one guinea pig were inoculated (infraperitoneal) with the patient's blood and treated in the same manner as in the search for trypanosome. Nineteen days later the inoculated guinea pig died. Spirochætæ were demonstrated from the profuse discharge from the nose and mouth, also a few from the bloodstream. The organisms from the nasal discharge were numerous, about seven to ten per high power field. The blood Wassermann was negative. It is of

interest to note that in some cases of the rat-bite fever it is positive. The white blood cell count was 16,000, with polymorphonuclears 65 per cent.

Treatment was started and .5 grams of sulpharsphenamine was given in the muscle at three-day intervals for four injections. The child was discharged cured on the fifty-third day.

Whenever there is a history of a bite by an animal, especially a rat, a blood-stream invasion by this organism should be kept in mind, and the case should not be discharged when the surgical wound has healed, but the patient should be kept under observation for the period of incubation.

To summarize, Rat-bite Fever is:

1. A disease caused by the bite of an infected rat.
2. It is characterized by a relapsing type of fever, with a moderate or severe toxemia, a characteristic xanthema, and a local inflammation at the bite area with adjacent lymph adenitis.
3. It is caused by the spirochæta morsus muris.
4. The incubation period varies from ten to twenty-eight days, with an average of two weeks.
5. The mortality has been placed at 10 per cent., but this should be lowered by treatment with salvarsan.

SUBACUTE PANCREATITIS OR SO-CALLED ACUTE ŒDEMA OF THE PANCREAS

Dr. DeWitt Stetten read a paper with the above title, for which, with discussion, see page 248.

BRIEF COMMUNICATION

INSULIN IN THE TREATMENT OF NON-DIABETIC BED SORES

INSULIN is a proven remedy in indolent ulcers. Decubitus is, for the most part, not only indolent but progressive. Due to the invasion of secondary infection, it is sometimes the direct cause of death in a lingering or exhausting disease. Since the introduction of insulin, occasion has arisen to use it by the reporter in five cases of decubitus in non-diabetic patients. The results were uniformly satisfactory.

CASE I.—Female, aged sixty-four, Para VI, has had cardiac trouble for over twenty years. There is a history of several decompensations and several nervous, bordering on mental, breakdowns. Albumin and casts were repeatedly found in the urine but never glucose. Wassermann negative. Eight weeks ago patient suffered from cardiac decompensation and mental breakdown. In addition there were cramps in the legs and intense pains in the course of the sacral and crural nerves. Hæmorrhoids which were always a complicative factor became more bothersome, and urinary and fecal incontinence became frequent of occurrence. A bed sore in the coccygeal region which developed about four weeks previously kept spreading and added greatly to the complexity of the situation. Scrupulous cleanliness and various ointments seemed to make no difference in the progress of the ulceration which by then occupied an irregular area of about three and one-half by two and one-half inches, was sloughy and deep. Through the courtesy of Dr. L. Spiegel, insulin injections were now instituted, fifteen units before dinner. Improvement began almost immediately and at the tenth injection the bed sore had diminished to about one-fifth its former size and had become quite superficial in depth. There was a marked improvement in the mental symptoms and the incontinence disappeared almost entirely. The tenth injection was followed by insulin shock, but was controlled by the administration of orange juice and sugar water. She received no further insulin for five days, but the decubitus kept progressively healing, when it was again instituted on alternate days. At the time of the fourteenth injection a pin-head opening was all that remained of the original sore.

CASE II.—Male, aged sixty-eight, suffering chiefly from cardiovascular disturbances. Wassermann negative. Blood sugar content on three different examinations averaged 160, and urine, over a period of one year, showed a trace of sugar (calculated as one-tenth of 1 per cent.). During an attack of apparent grippe the patient was put to bed. Sacral decubitus developed about two weeks later and one on the left heel about a week after that. Surgical cleanliness and ointments were of no avail. Patient was started on five units of insulin two times a day. A change for the better was noticeable on the third day, and on the eighth day, after the initial injection, the sacral sore was about half its original size; the heel sore remained stationary. Ten units (making a total of fifteen units a day) were then administered before the evening meal and the improvement became more noticeable still. The sore in the heel seemed to make even better progress than that in the sacrum. The general physical condition showed marked improvement, but inasmuch as other stimulating therapy was administered, the action of the insulin was duly discounted. The patient died of pulmonary œdema three months later, after being out of bed for more than a month prior to his death. The sacral bed sore was completely healed and only a very superficial and very small granulating surface remained under the left heel. The insulin treatment was

reduced to five units once a day for six weeks, and discontinued entirely four weeks prior to death.

Case III.—Female, aged fifty-eight, with a blood-pressure of 240/120 to 180/90, was diagnosed as luetic with apparent early paresis. Wassermann negative. Spinal puncture was not permitted. One of the pupils was immobile to light and the other reacted faintly. Knee-jerks could not be obtained (patient was then in bed). Urine always negative to sugar. A sacral bed sore developed rapidly after about ten days in bed in spite of excellent physical care. The mental symptoms, chiefly noisily irrational, increased in severity. Insulin injections, ten units once a day, were instituted, at which time the sore was about four inches in diameter, necrotic almost down to the bone. In less than two weeks the ulcer had decreased about one-half and healthy granulating tissue was everywhere present. There was a definite improvement in the mental status. In five weeks' time there remained but a small superficial ulcer. The mental condition was much improved. It is but fair to add that mixed treatment and mercurial inunctions were used at the same time. About one year later this patient died of a cerebral embolus.

Case IV.—Female, aged thirty-nine, with a pulmonary abscess following pneumonia. She was ambulatory for several months after a successful partial thoradectomy. Due to a fresh infection she was compelled to go to bed. Temperature ranged from 101° to 103.5°. Emaciation was rather rapid and a sacral decubitus developed in about three weeks' time. Spleen was enlarged. Diagnosis, proven by X-ray, was further pulmonary involvement in region of the first lesion. No sugar was found in repeated examinations of the urine. Bence-Jones' reaction positive. The decubitus at the time the insulin treatment was instituted was sloughy and about two inches in diametre. Dosage ten units once a day. In ten days' time it had all but disappeared. The general condition was distinctly improved (for about three days the temperature was normal, and appetite, which was very poor from the start, became normal). A new infection apparently again made its appearance and the patient died of exhaustion and in coma fourteen weeks after she went to bed. The decubitus never recurred, although its original site became bluish-black twenty-four hours before demise. There had been no insulin treatments for over six weeks before death.

Case V.—Probably the most rapid results were obtained in a female, aged sixty-two, suffering from a severe non-malignant cystitis. When for better control she was ordered to bed, she developed a small sacral and a larger left sacro-iliac sore. Insulin injections of fifteen units (divided in five and ten), daily, cured both in ten days' time. The sacro-iliac sore was one and one-half inches in its greatest width when the insulin treatment was begun. The cystitis immediately improved. There was partial incontinence before the patient went to bed, but due to the physical care it apparently did not enter as a factor in the development of the decubitus. The patient has remained well a year and a half after the last insulin treatment.

In all the above, other remedies had been used in addition to the insulin, but were for the most part discontinued as soon as the insulin was begun. With the exception of the patient with the pulmonary abscess, the others suffered clinically, at least, from degenerative vascular disease—the so-called arteriosclerosis. Experience with the treatment of decubitus in the presence of vascular degenerative disease is unpleasant at its best. An agent which modifies their course more favorably than any other treatment is apparently to be found in insulin.

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BOOK REVIEW

DISEASES OF THE URINARY TRACT IN CHILDREN. By EDWIN BEER, M.D., AND ABRAHAM HYMAN, M.D. Quarto; pp. 311; 50 illustrations. Paul B. Hoeber, New York, 1930.

THIS volume presents the personal experiences of the past twenty years of the authors in the study of diseases of the urinary tract in young children, representing mostly their observations in the wards of the Mt. Sinai Hospital. The subject is dealt with by them from a diagnostic, pathologic and therapeutic standpoint.

Diagnostic work in this field received very great impetus by the introduction to the surgical armamentarium of a child's cystoscope in 1907 which from then on placed the study of these diseases on a much more accurate basis, although not entirely commensurate with that obtained in the study of adults. Much effort has been made to show the conditions of the genito-urinary organs which have their incipiency in childhood but are not usually recognized until the second or third decades. The usual deformities of the genitalia which have heretofore been thoroughly recorded in the usual text-books are considered merely in their relation to the consequent damage in the urinary tract proper.

The book is comprised of fourteen chapters which represent the general pathologic conditions of the genito-urinary system as far as the bladder. Those considering the general symptoms and methods of examination well repay careful study. The introduction of uroselectan, while still in what might be called an experimental stage, has already proved its value in the diagnosis of pathologic conditions, particularly in children, while mechanical manipulation of the cystoscope and ureteral catheter has, at times, proved most difficult and unsatisfactory. The intravenous use of this chemical can be employed under conditions where no such armamentarium as is necessary can be obtained. Illustrations of this procedure are introduced into the book and are most instructive.

It is felt that the present work will unquestionably prove a definite stimulus to more extensive endeavor in the recognition of diseased conditions of the urinary tract in children, not only to the pediatrician, but also to the surgeon and to the urologist.

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EDITORIAL ADDRESS

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